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Original Communications

PERICARDITIS

Clinical and Laboratory Data of 130 Cases

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PERICARDITIS is one of the most commonly overlooked clinical conditions. The manifestations of both acute and chronic involvement of the pericardium may be primary or secondary. It behooves us, therefore, to review and analyze our case material from time to time. We must be alert to the signs and symptoms and diagnostic laboratory studies that will make for greater accuracy and fewer failures in the diagnosis of this lesion. This is especially desirable now that antibacterial and hormonal agents are offering more in the way of curative therapy and earlier and safer preparation for radical surgical treatment. Pericarditis for many years has been the subject of interest in our clinic and our cardiovascular research laboratories.[1]

Pericarditis is a somewhat uncommon clinical condition, yet it warrants reconsideration at this time. Griffith and Wallace[2] recently analyzed 1,000 post-mortem cases autopsied over a period of ten years, which showed evidences of pericarditis. They pointed out that pericarditis was found in 5.8 per cent of their autopsy series; this was twice the incidence in clinical practice. Furthermore, there were noted changes in the incidence of certain etiological types as compared with the data reported twenty years ago by Smith and Willius[3] and that reported fifty years ago by Preble.[2]

In recent years bacterial pericarditis, including the tuberculous type, has decreased, while pericarditis secondary to cardiovascular disease, uremia, and malignancy has increased with the increase in the life span of the population. Carmichael, Sprague, Wyman, and Bland[4] have restudied their fifty acute, nonspecific, or virus pericarditis cases and emphasized the apparent increase in the condition, the characteristic clinical picture, and the excellent long-term prognosis.

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Peel[5] felt that the incidence of tuberculous pericarditis was underestimated and that many early cases were overlooked. He treated his eight cases conservatively without streptomycin and reported good results. Constrictive pericarditis developed in only one patient who was operated upon and died six months later. We have observed two cases of tuberculous pericarditis treated with streptomycin. One of these patients after many months of invalidism had a successful decortication. The other patient had a pericardiectomy performed early after streptomycin therapy, and he had a much less stormy course and earlier rehabilitation. Consideration of these specific cases and others led us to a survey of all of our cases of pericarditis during the past five years.

MATERIAL

The case records of all patients in the University of Texas Hospitals who had been diagnosed as having pericarditis during the five-year period, 1946 through 1950, were carefully reviewed. One hundred and thirty cases, eighty-nine proved at autopsy and forty-one during life, were selected for detailed analysis. This included only those cases in which the diagnosis of pericarditis was substantiated at autopsy (eighty-nine cases), by surgical operation, or by the diagnostic finding of pericardial fluid, a pericardial friction rub, pathognomonic radiologic evidence or electrocardiographic changes, or an unquestionable combination of significant signs (forty-one cases). In most of these the pericarditis was of clinical importance, and in many it was contributory to death.

TABLE I. AGE INCIDENCE IN PERICARDITIS

AGES (YRS.)	NO. OF CASES
0 to 9	8
10 to 19	13
20 to 29	22
30 to 39	20
40 to 49	18
50 to 59	18
60 to 69	19
70 to 79	9
80 to 89	3
Total Cases	130

Sex: Male—85; Female—45.
Race: White—63; Negro—67.

The incidence was greatest in the male sex (eighty-five men and forty-five women). Of the one hundred-thirty cases sixty-three were Caucasian and sixty-seven were Negro patients. No age group seemed to be particularly affected with pericarditis, each decade from 20 to 70 years accounted for about twenty cases, as is shown in Table I.

The etiological factors and the pathologic data are shown in Tables II, III, and IV. Pyogenic organisms and uremia were the most common causes; idiopathic pericarditis was next; the others occurred in the following order:

epistenocardiac, fifteen cases; malignancy, thirteen cases; rheumatic fever, fourteen cases; tuberculosis, eleven cases; collagenous disease, five cases; and trauma, five cases.

Table II. Etiology and Pathology

	NO. OF CASES		NO. OF CASES
Septicopyemia	23	Tuberculous	11
Pyogenic	20	Effusion	4
Amebic	1	Hemorrhagic	1
Coccidioidomycosis	1	Fibrosis	4
Blastomycosis	1	Constrictive	2
Traumatic	5	Idiopathic	17
Purulent	1	Fibrinous	9
Hemorrhagic	2	Effusion	3
Telangiectasia	1	Fibrous Adhesive	3
Dissecting Aneurysm	1	Hemorrhagic	1
		Constrictive	1

Table III. Etiology and Pathology

	NO. OF CASES		NO. OF CASES
Rheumatic	14	Uremic	24
Fibrinous	7	Fibrinous	21
Effusion	2	Effusion	2
Fibrous	5	Hemorrhagic	1
Epistenocardiac	15	Malignant	13
Fibrinous	4	Adenocarcinoma	10
Fibrous	8	Sarcoma	3
Ruptured	3		

Table IV. Etiology and Pathology

	NO. OF CASES		NO. OF CASES
Collagenous	5	Tamponade	10
Polyarteritis	1	Ruptured Heart	3
Effusion Lupus erythematosus	4	Dissecting Aneurysm	1
3 Fibrinous		Pyogenic	3
1 Fibrous		Tuberculous	1
		Idiopathic	1
		Adenocarcinoma	1

The symptoms and signs were quite variable; they are summarized in Table V. Pain was complained of in sixty of the cases, dyspnea in fifty-one, cough in eighteen, and syncope in only six cases. Fever was significant in forty-seven; polymorphonuclear leukocytosis in thirty-four. A pericardial friction rub was heard in thirty-four and distant heart sounds with an accentuation of the P_2 in

fifteen cases; a gallop rhythm was recorded only occasionally. Cyanosis occurred in seven cases and posterior left pulmonary base dullness was found in ten cases. The liver was palpable in eleven cases and the venous pressure was found elevated in seven cases. Radiologic (Table VI) diagnostic signs of pericarditis were found to be present in twenty-two cases and suggestive signs were present in an additional thirty-seven cases; normal findings were present in eighteen cases and no films were made in the remaining fourteen (Table VI). Electrocardiographic findings were diagnostic of pericarditis in thirty-five cases and suggestive in an additional forty-seven (Table VI). No electrocardiograms were done in nineteen patients, and it is significant that the tracings were within normal limits in only seven.

TABLE V. SYMPTOMS AND SIGNS

	NO. OF CASES		NO. OF CASES
Pain	60	Dullness	43
Chest	40	Anterior Heart	33
Epigastric	13	Posterior Lung	10
Neck and Back	7	Both Posterior and Anterior	6
Pericardial Friction Rub	34	Enlarged Liver	11
Fever	47	High Nonprotein Nitrogen	24
Cyanosis	7	Dyspnea	51
Distant Heart Sounds	15	Cough	18
Leukocytosis	34	Syncope	6

TABLE VI. SPECIAL DIAGNOSTIC METHOD

RADIOGRAPHY	NO. OF CASES	ELECTROCARDIOGRAPHY	NO. OF CASES
Suggestive	37	Suggestive	47
Diagnostic	22	Diagnostic	35
No Evidence	39	No Evidence	22
Not Done	14	Not Done	19
Normal	18	Normal	7

ELECTROCARDIOGRAPHIC DATA

The electrocardiographic changes of pericarditis have been mistaken for those of myocardial infarction; however, significant differences are easily demonstrable. Electrocardiographic data from our cases are set down in Table VII. The S-T segment changes of pericarditis are the most characteristic, particularly elevation of the S-T segment and the concave upstroke of the T waves. In general, negativity of the T wave does not develop in uncomplicated acute pericarditis and, in the chronic stages, appears only after the S-T segment drops down to or below the isoelectric line. However, in one case of acute trauma in this series, T negativity developed with S-T elevation. Q waves of myocardial infarction are never present in uncomplicated pericarditis. In four of our cases of epistenocardiac peri-

carditis with signs of myocardial infarction, the prominent concave S-T elevations suggesting the complicating pericarditis were found.

Serial electrocardiographic changes are of great value in diagnosis, particularly when the evolution progresses rapidly as it usually does in pericarditis. This evolution was found to be rapid in twenty-eight cases in our studies.

Table VII. Electrocardiographic Changes in 111 Cases of Pericarditis

	NO. OF CASES
Diffuse acute subepicardial injury (S-T elevation, concave in Leads I, II, III, aV_L, aV_F, and V)	15
Acute myocardial infarction with prominent concave S-T elevation suggesting complicating pericarditis	4
Negative or low T in Leads I, II, III, aV_L, and V	26
Acute subepicardial injury anteriorly (S-T elevation, concave up in Lead I; at times II and aV_L, and one or more in V_1 to V_6)	13
Changes (elevation S-T, negative T, etc.) confined to one or more of precordial leads	6
Negative T in leads only from anterior surface (Leads I, II, aV_L, V)	8
Acute subepicardial injury posteriorly (S-T elevation in Leads II, III, aV_F; at times V_5 and V_6)	4
Electrocardiographic serial changes	28
Low voltage QRS and T	28
Negative T in leads only from posterior surface (Leads II, III, aV_F; at times V_5 and V_6)	2

Evidences of diffuse acute subepicardial injury (S-T elevation, concave in Leads I, II, III, aV_L, aV_F, and V) were found in fifteen cases with relatively rapid return to the isoelectric line; negative T waves developed with no definite Q wave changes except in the infarction cases. Acute subepicardial injury anteriorly (S-T elevation, concave up in Leads I and at times II, aV_L, and one or more in V_1 to V_6) appeared in thirteen cases. Acute subepicardial injury posteriorly (S-T elevation in Leads II, III, aV_F, and at times V_5 and V_6) appeared in four cases. Subacute diffuse changes as negative or low T in Leads I, II, III, aV_L, and V were present in twenty-six cases. Chronic changes as low-voltage QRS and T appeared in twenty-eight cases of pericarditis. Subacute subepicardial injury with negative T in leads only from the anterior surface (Leads I, II, aV_L, and V) developed in eight cases.

REVIEW

A review of these data and recent literature on pericarditis, along with the study of the records of our last 130 cases, reaffirmed some of our concepts and added new emphasis and ideas on other phases of the subject.

Acute purulent pericarditis was found to develop usually during severe infection or after penetrating trauma. The primary clinical condition often dominated the picture. Acute idiopathic or nonspecific pericarditis appeared two or three weeks after acute upper respiratory infections. Acute rheumatic pericarditis likewise followed beta hemolytic streptococcus sore throat after several weeks. Acute nonspecific type had been considered to be of virus origin since some cases have apparently responded to aureomycin. Then too, like rheumatic fever, it may have been an allergic reaction of serous membrane sensitization as suggested by McKinley.[6]

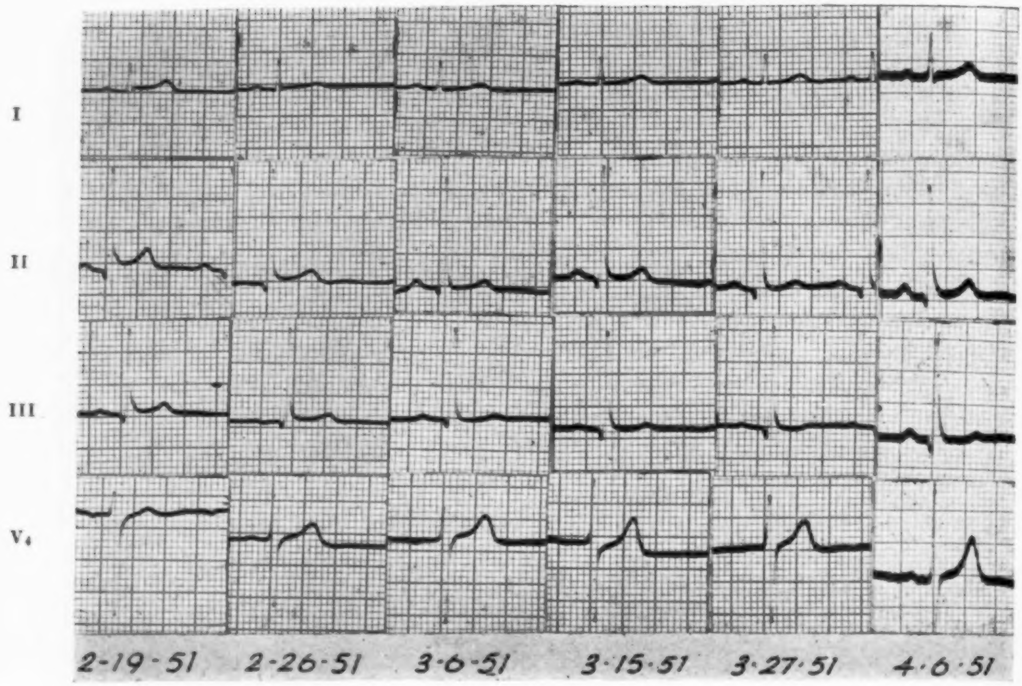


Fig. 1.—(G. R. J., 36 years old.) Electrocardiograms showing S-T segment elevations and a clinical picture of severe pain, erroneously diagnosed as coronary occlusion and myocardial infarction two weeks after an upper respiratory infection.

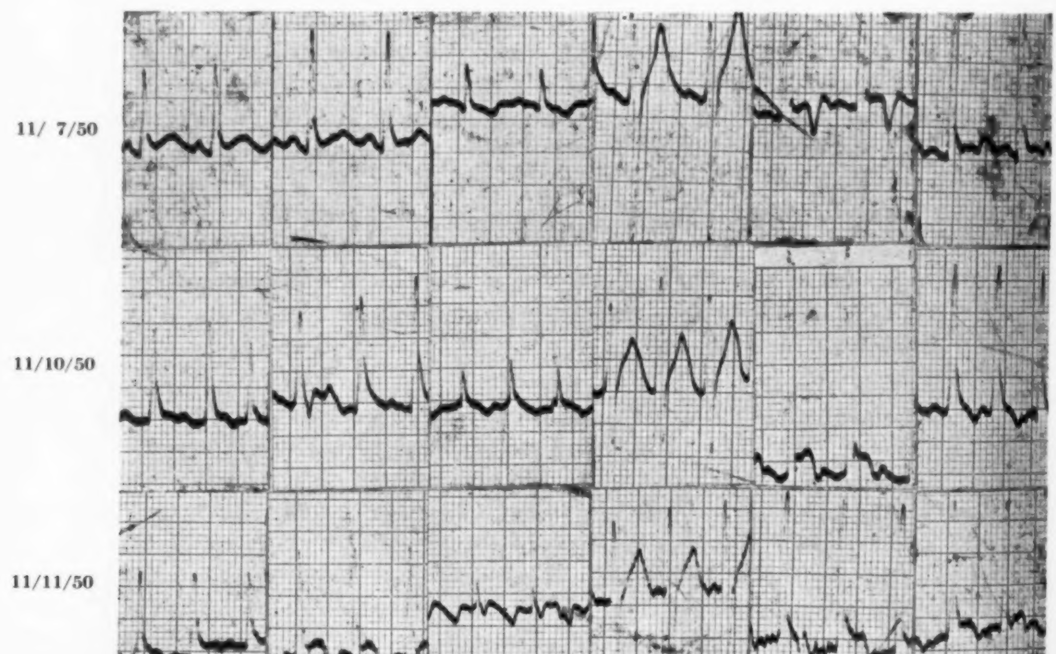


Fig. 2.—(J. C. S., 60 years old.) Electrocardiograms indicating pericarditis which was proven to be purulent in nature on pericardial paracentesis, and fibrinopurulent at operation.

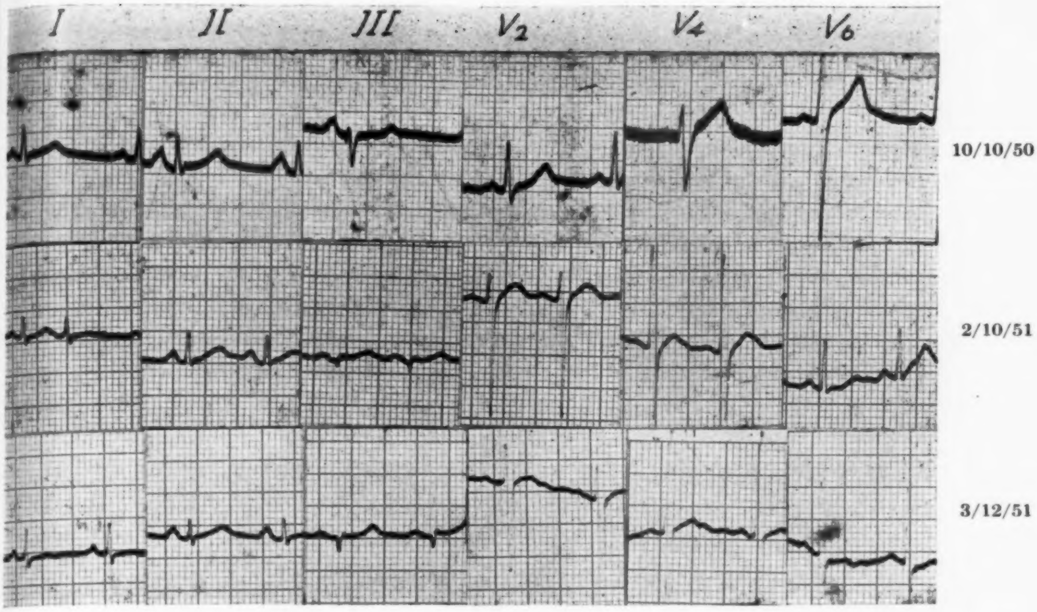


Fig. 3.—Electrocardiograms on E. R., 58 years old, who had fever of unknown origin, with "negative" radiograms but changes suggestive of pericarditis. Pericardial paracentesis yielded an exudate which proved to contain tubercle bacilli.

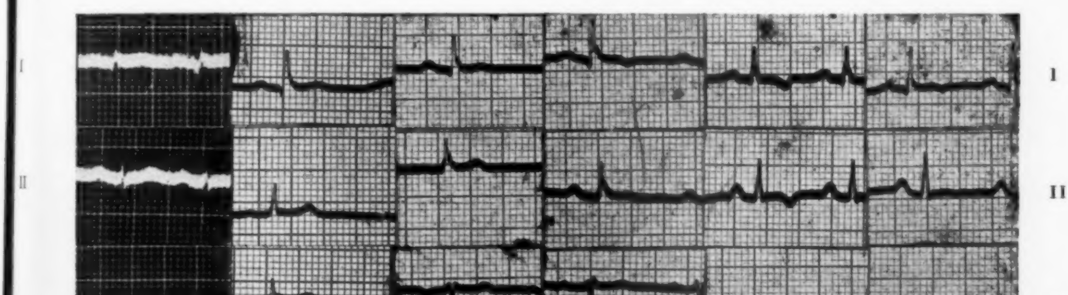


Fig. 4.—Electrocardiograms on J. G., 24 years old, with subacute recurrent pericardial exudation, tamponade, and syncope. The pericarditis was proved to be tuberculous in nature, treated with streptomycin and para-aminosalicylate; pericardiectomy (8/24/50) with recovery.

Microorganisms are responsible for a large proportion of cases of pericarditis; other etiologies must be considered, however. Myocardial infarction, trauma, myxedema, uremia, lupus erythematosis, polyarteritis, and primary and secondary malignancy were etiological factors to be reckoned with in the differential diagnosis. Primary acute tuberculosis of the pericardium was fairly common, and fungus pericarditis occurred. Acute syphilitic pericarditis has been uncommon in our experiences. Secondary types of pericarditis were most commonly bacterial in origin but occasionally the etiology was fungus invasion or malignant infiltration.

12/12/49 12/17/49

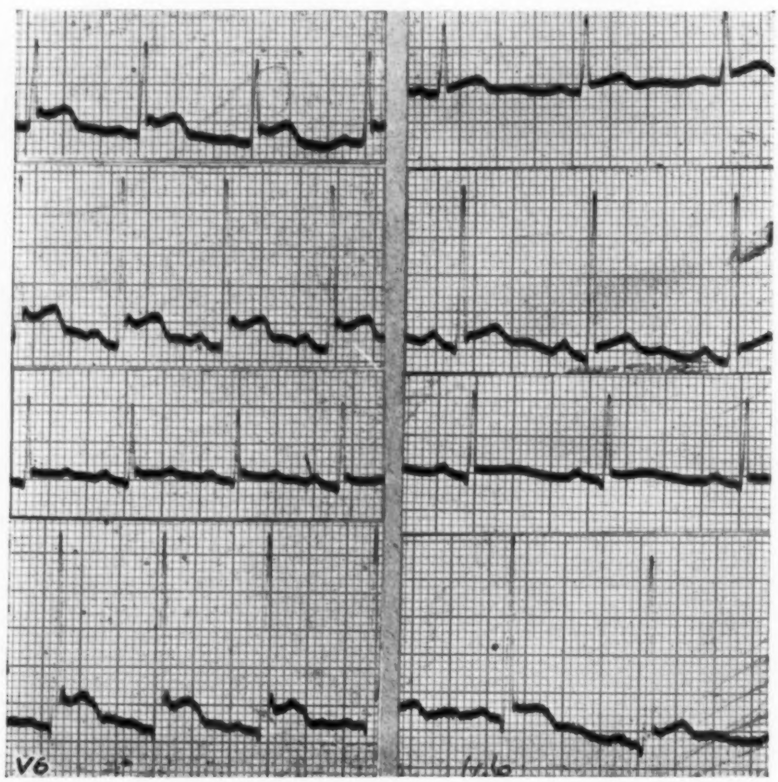


Fig. 5.—Electrocardiograms on R. B., 21 years old, with stab wound and cardiac tamponade relieved by tapping; spontaneous healing without recurrence.

Symptoms and physical signs depended to some extent upon the inflammatory processes that were present in the pericardium, the state to which it had developed, and the local circumstances and reaction.

The cardinal symptoms were malaise, chills, fever, cough, dyspnea, orthopnea, and pain. The pain was usually sharp, dull, gripping, aching, constricting and pressing, and usually radiated to the neck, left shoulder, and arm, interscapular and epigastric regions. Pain was aggravated by inspiration if the adjacent pleura was involved.

The physical signs revealed the diagnostic criteria, the most significant of which was the pericardial friction rub. The friction rub might have been early

and widespread; usually it was variable and persisted in some instances only over the pulmonary conus. The friction rub was occasionally present over the whole precordium and back and was sometimes accompanied by friction fremitus. A diastolic pulmonic shock and accentuated P_2 was usually felt, and the heart sounds were often suppressed. Cardiac tamponade of severe degree produced engorgement of the neck veins, paradoxical pulse, atelectatic compression of the left lower lobe, occasionally complicated by pleural effusion. Removal of fluid by paracentesis with a prompt decrease in the cardiac outline and with pleural sacs clear of the fluid was considered diagnostic. The etiological factor was often revealed by careful laboratory study of the fluid, including culture and imbedding the sediment, and blocking for section and microscopic examination.

Clinically, pericarditis is considered to be acute, subacute, or chronic in type, and may be active or healing. Pathologically, there may be fibrinous, exudative, serous, gangrenous, purulent, adhesive (partial or complete synechia anchoring parietal or mediastinal pericardium), and constrictive pericarditis.

The primary nonspecific infectious type could have been questionably virus, questionably toxic, questionably allergic in origin since it followed upper respiratory infections. This could be etiologically similar to that of rheumatic fever, of polyarteritis nodsa or of lupus erythematosus disseminata. Primary noninfectious pericarditis was myxedematous, uremic, and primary malignant in origin.

Secondary pericarditis was infectious, tuberculous, malignant, pyogenic pneumonococcic from pneumonia, general sepsis, mediastinitis, mycotic, hemorrhagic from a weeping dissecting aneurysm or due to metastatic malignancy. Coccidioidomycosis, actinomycosis, blastomycosis, streptothrix, and amebiasis have resulted in involvement of the pericardium. They may have been implanted through the blood stream or have penetrated from the contiguous granuloma.

Hemorrhage from traumatic myocardial contusion, gunshot wounds, stab wounds penetrating into the pericardium severing a coronary vessel, and ruptured dissecting aneurysm have induced pericarditis.

Epistenocardiac pericarditis was the result of myocardial infarction involving epicardial surface of the heart. Pneumopericardium resulted from the injection of air after removal of fluid, and very rarely the air may have come from mediastinal emphysema due to a ruptured emphysematous bleb, the trachea, or from gas-producing bacteria in the pericardium.

The anatomic diagnosis depended upon the localization, the acuteness, or chronicity and type of etiology. The lesion was circumscribed or patchy over the anterior or posterior surface, generalized or diffuse over the whole epicardium. There was extension to or through the parietal as well as the visceral pericardium. The subacute type of involvement was fibrinous, serous, hemorrhagic, purulent, or combinations of these. Acute and subacute pyogenic infection usually produced the fibrinous cor villosum or shaggy heart. Multiple serositis or Pick's syndrome[9] was usually associated with pleuritis and peritonitis. This must be differentiated from the hydropericardium and hydrothorax and ascites of heart failure.

8/24/50—P.M.

8/24/50—A.M.

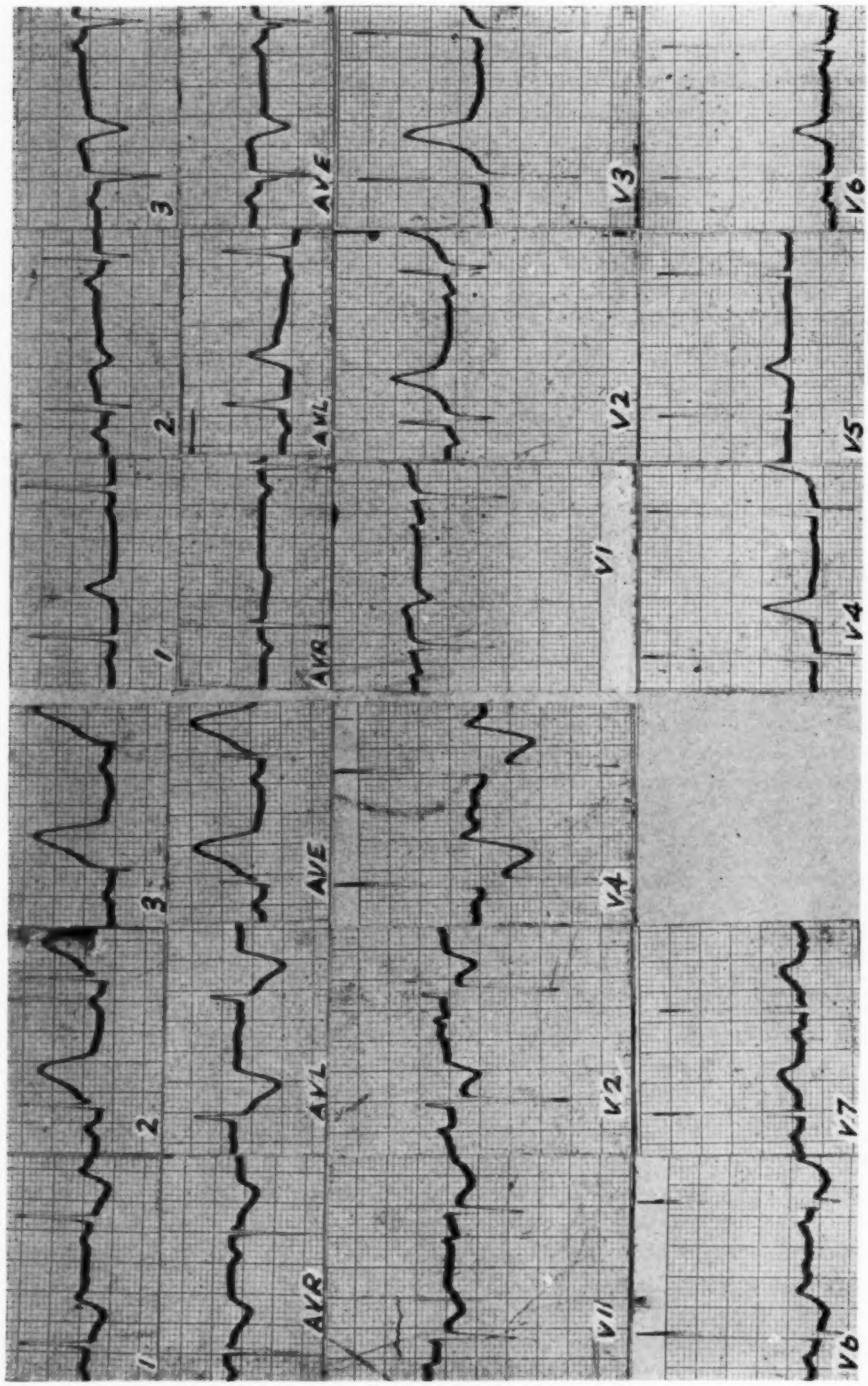
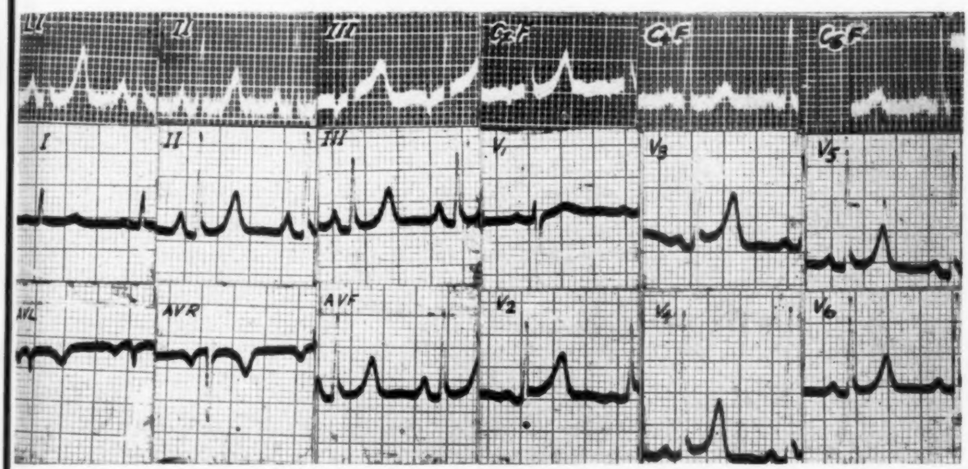


Fig. 6.—Electrocardiograms on J. C. C., 55 years old, with acute posterior myocardial infarction and pericarditis.

In the subacute stages of chronic fibrinous to fibrous involvement, adhesions formed resulting in partial to complete obliteration of the pericardial cavity. When the parietal pericardium was penetrated, involvement of the pleura resulted with adhesions to the diaphragm and to the chest wall. Adhesions caused embarrassment of the heart action. Complete synechia of the pericardial cavity usually resulted in constriction and a small heart with restricted movement, a large liver, and ascites. Anchoring extra precardial adhesions, mediastinopericarditis of Concato's syndrome contributing to cardiac hypertrophy, was probably of rheumatic origin or the aftermath of chronic healing tuberculosis. Calcium deposition in plaques or as a shell about the heart shown in the radiologic films was considered an absolute diagnostic sign of chronic pericarditis, but not necessarily of constrictive pericarditis.[10]



10/31/47

7/27/50

Fig. 7.—Electrocardiograms on M. L., 54 years old, with hemorrhagic pericardial effusion as a result of carcinomatous metastases from carcinoma of the esophagus.

THE CLINICAL DIAGNOSIS OF PERICARDITIS

Pericarditis must be considered as a possibility, in obscure conditions, if it is to be recognized as often as it occurs. The history or findings of etiological conditions that commonly cause pericarditis should alert the physician and render the condition open to suspicion. The clinical case study may or may not reveal an etiological factor and sometimes extensive clinical investigation may fail to reveal the genesis.

The cardinal symptom of pain or distress may be characteristically propagated to the left shoulder or neck or may be only a vague distress in the precordium or the epigastrium. Dyspnea may be the equivalent of, substitute for, or may follow the pain. The pathognomonic sign is the pericardial friction rub which may often be felt or heard when the breath is held in expiration. Bulging of the precordium or the intercostal spaces or distention of the neck veins may be noted. The sharply demarcated and widened cardiac or upper retrosternal dullness is rarely demonstrable. The auscultatory finding of the friction rub

Fig. 6.—Electrocardiograms on J. C. C., 55 years old, with acute posterior myocardial infarction and pericarditis.

and/or very distantly muffled heart sounds are the most reliable clinical signs. Further data obtained by fluoroscopy, teleradiography, kymography, electrokymography and electrocardiography are the most acceptable accessory diagnostic aids.

CONCLUSIONS AS TO TREATMENT

The treatment of pericarditis is determined by the etiological factor and the anatomic changes that have been established. Antibiotics used against primary infection often prevent and/or abort a pericarditis. Serous effusions only occasionally require paracentesis. Purulent exudate usually requires surgical drainage. Two cases of tuberculous pericarditis have convinced us that pericardiectomy should be considered early, immediately after a course of streptomycin and PAS therapy. Aureomycin may be considered as worthy of trial in patients with acute idiopathic or nonspecific pericarditis.

REFERENCES

1. Herrmann, G. R., and Schwab, E. H.: Electrocardiographic Changes in Acute and Chronic Pericarditis. Experimental Studies, Proc. Soc. Exper. Biol. & Med. **31**:1050, 1931; Some Experimental and Clinical Electrocardiographic Observations on R-S-T and T Changes in Pericarditis, Tr. A. Am. Physicians **49**:229, 1934.
   Herrmann, G. R., and Ochsner, Alton: Arch. Surg. **18**:365, 1929; Proc. Soc. Exper. Biol. & Med. **25**:763, 1928.
   Herrmann, G. R., and Musser, J. H.: Experimental Pericarditis, Tr. A. Am. Physicians **43**:23, 1928; Proc. Soc. Exper. Biol. & Med. **25**:314, 1928.
2. Griffith, George, and Wallace, L.: The Etiology of Pericarditis. Personal communication, 1951.
3. Smith, H. L., and Willius, F. A.: Pericarditis, Arch. Int. Med. **50**:171, 184, 192, 1932.
4. Carmichael, D. B., Sprague, Howard B., Wyman, S. M., and Bland, E. F.: Acute Nonspecific Pericarditis, Circulation **3**:321, 1951.
5. Peel, A. A. F.: Tuberculous Pericarditis, Brit. Heart J. **10**:195, 1948.
6. McKinlay, C. A.: Allergic Carditis, Pericarditis, and Pleurisy, Journal Lancet **68**:61, 1948.
7. Barnes, A. R., and Burchell, H. B.: Acute Pericarditis Simulating Acute Coronary Occlusion, Am. Heart J. **23**:247, 1942.
8. Bellet, S., and McMillan, T. M.: Electrographic Pattern in Acute Pericarditis, Arch. Int. Med. **61**:381, 1938.
9. Kelly, A. O. J.: Multiple Serositis, Am. J. Med. **125**:16, 1903.
10. Harrington, S. W.: Chronic Constrictive Pericarditis; Results of Partial Pericardiectomy and Epicardiolysis in 34 Cases, Mod. Concepts Cardiovas. Dis. **16**: May, 1947.

LYMPHOCYTOPENIA IN HEART DISEASE

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In a previous paper,[3] it was reported that in coronary infarction there is often a marked decrease in the absolute lymphocyte count. This investigation had been undertaken to establish whether variations in the white blood cell count occur in the course of arteriosclerosis. Cases of coronary infarction had been chosen for study although it was realized that a small number of these cases might have been caused by conditions other than arteriosclerosis and that in a few instances the arteriosclerosis might be restricted almost entirely to the coronary vessels. In such cases therefore the white blood cell picture might not be truly representative of arteriosclerosis.

In that report the number of cases studied was relatively small so that the findings had to be treated with caution, but additional studies have confirmed the earlier observations so that it seems advisable to publish the complete findings.

The average lymphocyte count and its normal range have not been finally determined. For some authorities the range is very wide, for others narrow. The "normal" proportion of lymphocytes has been commonly given as 20 to 25 per cent. More recently, this has been raised to 30 per cent, and several authors now consider 25 to 40 per cent (Osgood and Ashworth;[23] Augarten[4]) or 35 to 45 per cent (Castelle-Rothe[7]) as normal limits. The last named author in 174 healthy persons found none with less than 30 per cent. Branscheid and Erhardt[6] give even 33 to 47 per cent as normal, with a mean of 40 per cent. These percentages by themselves give no indication of the absolute number of lymphocytes in any given case. They are, therefore, almost valueless unless the total count is also given since there is no universally accepted standard, and there is much individual variation. The "normal" lymphocyte count is usually given as 2,000 to 3,000 per cubic millimeter although some authors give 1,500 as the lower limit and 4,000 as the higher. Schilling[28] accepts 1,050 and Boerner[5] even 1,000 as lowest limit of the "normal." Elmadjan and Pincus (1946)[15] made six lymphocyte counts at regular intervals throughout the whole day on each of twelve normal persons. The lowest lymphocyte count was 1,430 per cubic millimeter, the highest 5,570. In another study[24] on eleven normal persons these authors found 2,020 lymphocytes per cubic millimeter as the lowest and 5,417 as the highest count.

There are also physiologic variations due to age, such as the generally accepted and considerable lymphocytosis of early life and a much discussed varia-

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tion in old age. Many authors record a moderate lymphocytosis of old age (Augarten;[4] Aberg and Tötterman;[1] Corell[9]), while Weidenreich[31] reported a decrease from 31.6 per cent to 20.4 per cent between 67 and 81 years and Vallastro[30] a decrease of 4.1 per cent in the third and fourth decades and in the aged (60 years and over). On the other hand, some authorities maintain that age has no influence whatever on the white blood cell count (Stieglitz[29]). There are also geographic differences: For instance, the lymphocyte count of people living in Europe differs from that of people living in China. That this is not a racial difference is shown by the fact that Chinese living in Europe show the European formula (Augarten[4]). The influence of a maritime climate is believed to be the cause of differences between the lymphocyte counts of people living in Copenhagen and in Berlin (Augarten[4]). Even lesser geographic differences (e.g., between Berlin and Jena) are reported to influence the lymphocyte count (Castelle-Rothe[7]). Altitude seems to modify it, as do pregnancy, the climacteric, exposure to the sun, and exposure to cold. However, none of these fluctuations extends beyond the accepted physiologic range. Reports on the effect of ingestion of glucose are contradictory. Freeman and Elmadjan,[17] Marks and associates,[21] and Lazarus and co-workers,[20] report a depression, Castelle-Rothe[7] a lymphocytosis.

Few authors deal with lymphocytopenia as a pathologic feature, and some standard texts and handbooks of hematology do not even index it (Kracke;[19] Downey;[11] Hirschfeld and Hitmair[18]).

Lymphocytopenia of pathologic significance is reported in all types of aplastic anemia, pernicious anemia, Banti's disease, anemia due to liver cirrhosis, thrombosis of the portal vein (Osgood and Ashworth[23]), and Hodgkin's disease (Wintrobe[33]). Fever first causes lymphocytopenia, followed by lymphocytosis (Naegeli;[22] Castelle-Rothe[7]). The occasional drop in the number of lymphocytes during septic hyperleukocytosis is of ominous significance (Naegeli;[22] Schilling[28]). Marked lymphocytopenia also follows extensive destruction of lymphatic tissue.

De la Balze, Reifenstein, and Albright[10] in ten cases of Cushing's syndrome found two patients with less than 1,000 lymphocytes per cubic millimeter (630 and 384, respectively) and a low average of 1,500, 13.1 per cent for all cases. They concluded that "lymphocytes are rarely found to be decreased" and a "persistent lymphopenia should suggest Cushing's syndrome."

Reports of lymphocyte counts under 1,000 per cubic millimeter are not infrequently encountered in general readings. Rosenthal,[26] in a report on twenty patients suffering from a variety of severe conditions, mentioned a patient with Hodgkin's disease with 216 lymphocytes out of a total white blood cell count of 900; two patients with liver cirrhosis, one with 576 lymphocytes out of 3,200 white blood cells, the other with 800 out of 4,000 white blood cells; and one with nutritional anemia who had 950 lymphocytes out of 3,800 white blood cells. Reich and Reich[25] in ninety-four blood counts of seventeen nonleukemic patients found five with lymphocyte counts between 320 and 984. There are, certainly, many other reports of lymphocytopenia scattered in the world literature.

Although there are numerous reports on the total leukocyte count in coronary infarction, I was unable to find any reference to the absolute or relative number of lymphocytes, with the exception of one publication by Altana and Pulino.[2] In addition to the total white blood cell counts, these authors reported the relative

number of lymphocytes in various cardiac diseases, but ignored the frequent absolute lymphocytopenia found in their material, particularly in myocardial sclerosis. From their percentages we calculated the absolute number of lymphocytes and found numerous cases of severe absolute lymphocytopenia (Fig. 5).

RESULTS

Figures showing the absolute or the relative average number of lymphocytes for a group of individuals, even if supplied with the standard error, fail to give the average reader a clear picture of the deviation from normal, widely as this latter might be accepted. Such deviations are better and more simply presented in a diagrammatic way, as has been done in the following.

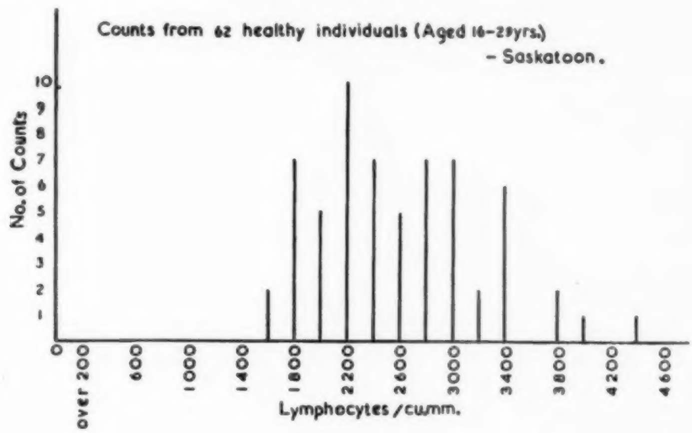

Fig. 1.

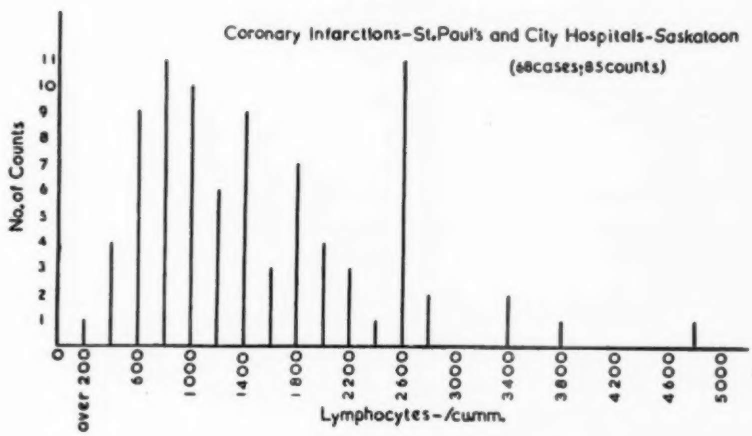

Fig. 2.

Since some patients had several counts done with great variations between the individual counts, in the following the total number of counts made has been given in addition to the number of cases. The first graph (Fig. 1) presents the absolute lymphocyte counts from a group of sixty-two healthy young individuals (medical students and technical personnel) taken between 9 and 10 A.M.

in Saskatoon. The average number of lymphocytes was 2,675 per cubic millimeter, with a standard error of ± 55. The second graph (Fig. 2) gives the lymphocyte counts of patients suffering from myocardial infarction taken from the charts of St. Paul's and City Hospitals, Saskatoon.* The average count was 1,612 per cubic millimeter, with a standard error of ± 67.5. The ages of the patients ranged from 47 to 89 years with an average of 62 years. The great majority died of the myocardial infarction and so provide a group of very severe cases. Fig. 3 gives 172 lymphocyte counts on 134 patients with coronary infarction in the Metropolitan Hospital, Welfare Island, N. Y.† In this group the average lymphocyte count was 2,430 per cubic millimeter, with a standard error of ± 60.8.

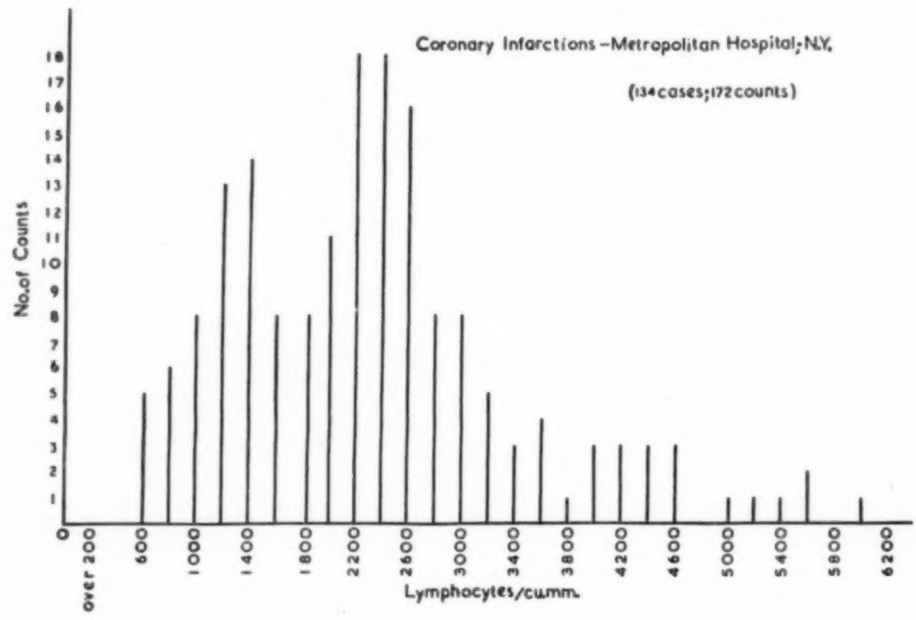

Fig. 3.

There is a considerable difference between the results obtained in the local cases and those found in the Metropolitan Hospital. It may be at least partly explained by the fact that most of the cases from Saskatoon (62 out of 68) were "autopsy cases." On the other hand, there was a higher incidence of lymphocytosis in patients of the Metropolitan Hospital, due probably to concomitant diseases. Fig. 4 combines the two groups from Saskatoon and New York and was computed to arrive at a less variable result.

It might be suggested that the lymphocytopenia observed in these patients with heart disease has been caused by the administration of drugs. Although a number of patients with low lymphocyte counts had received morphine and atropine or barbiturates before the blood samples had been taken, in an equal or even larger group no drugs whatever had been given previous to the examination.

It is well known that patients with coronary infarction, particularly the

*Courtesy Dr. D. F. Moore and Dr. J. W. Adams.
†Courtesy Dr. L. J. Boyd and Dr. E. Lifshutz.

severe cases, show marked neutrophilia. No clear relation between marked lymphocytopenia and neutrophilia could be shown in our cases.

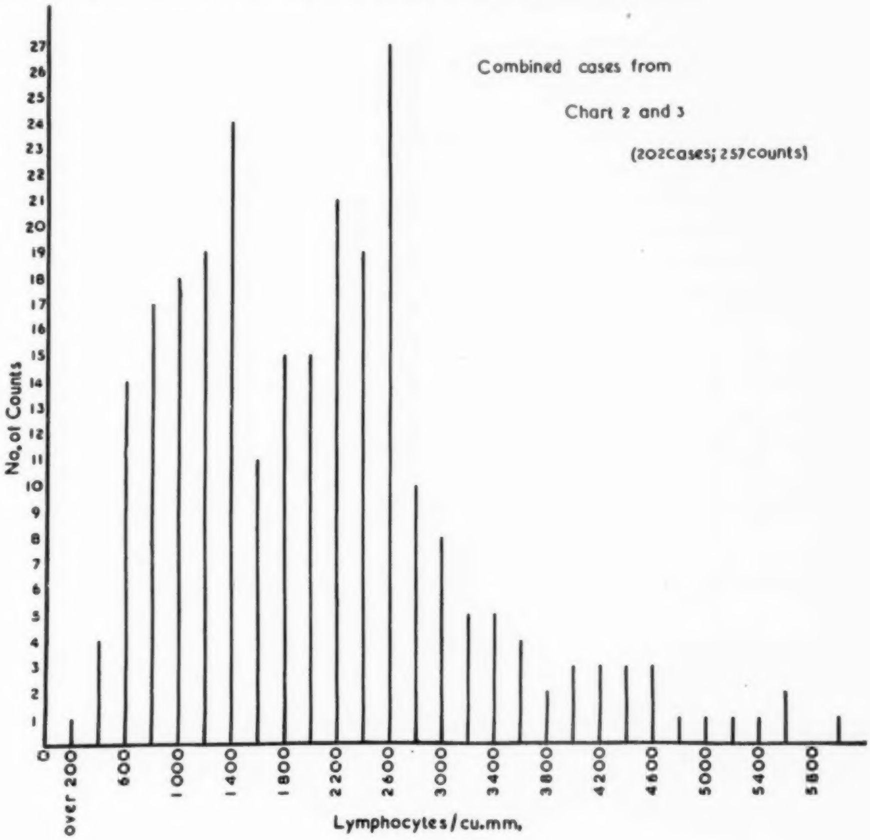

Fig. 4.

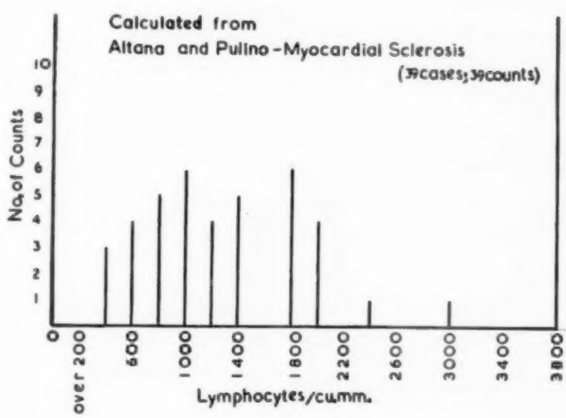

Fig. 5.

As mentioned before, Altana and Pulino[2] have reported on the white blood cell picture in various heart diseases including myocardial sclerosis. While a

significant proportion of the whole group showed lymphocytopenia, those with myocardial sclerosis showed a relatively larger number with low lymphocyte counts or outright lymphocytopenia (Fig. 5).

To compare myocardial lesions with other types of heart diseases, patients with decompensated rheumatic heart disease and with hypertension were also examined. In both groups were numerous patients with low or very low lymphocyte counts (Figs. 6 and 7). Obviously, the cases of hypertension may include a proportion of patients with "silent" myocardial lesions.

Finally, the blood findings in fifty-two patients 60 years or older, hospitalized for hernia, were examined. These provided a better control than our first group (Fig. 1) since they were similar in age to the patients with coronary disease and were exposed to the same psychologic effect of the hospital atmosphere.

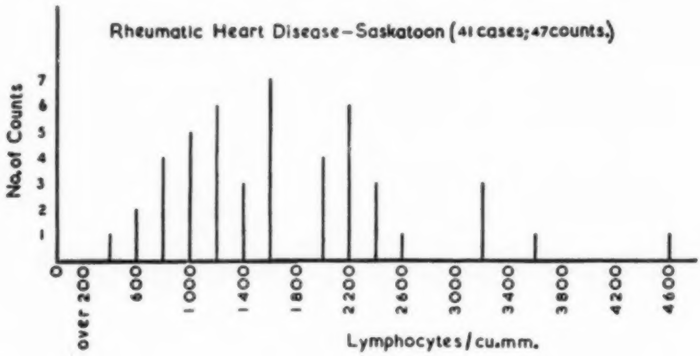

Fig. 6.

Fig. 7.

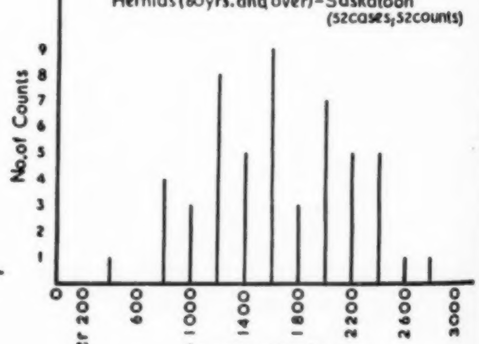

Fig. 8.

In this group (Fig. 8) there also were some low lymphocyte counts, which may be partly due to the psychologic "stress" of the hospital milieu, partly to the higher age or to some heart insufficiencies. Of nine patients with strangulated hernias, three had a lymphocyte count below 1,000, while of the other forty-three patients with simple hernias only two had less than 1,000 lymphocytes per cubic millimeter. The number of cases is too small, however, to permit any definite conclusion.

Unfortunately, we were unable to secure significantly large numbers of lymphocyte counts from old people in good health or from young people under the psychologic stress of hospitalization but without diseases which might affect the lymphocyte count.

DISCUSSION

Neither in our own material nor in the literature have we found in healthy people anyone with a lymphocyte count less than 1,000 per cubic millimeter.

In our survey, lymphocytopenia of less than 1,000 cells per cubic millimeter was found relatively often in cases with myocardial infarction, decompensated rheumatic heart disease, and hypertension and less frequently in old people hospitalized for hernia operation. The problems are (a) whether marked lymphocytopenia has a pathologic significance, (b) why it occurs only in certain periods of the disease, (c) whether it is due to stress, to circulatory disturbances, or to other factors. Coarse technical "errors" can be generally ruled out as an explanation of the findings since careless technicians would be inclined to give normal rather than unusual figures. As to (a), the absence of lymphocytopenia with values below 1,000 lymphocytes per cubic millimeter in normal individuals, as noted by Pincus and Elmadjan,[15] in our own group, and apparently in Castelle-Rothe's material,[7] and its relatively frequent occurrence under pathologic conditions make it likely that marked lymphocytopenia has a definite pathologic significance. As to (b), it is not clear why it may be present at one time and absent at other times in the same patient. As to its pathogenesis (c), we know from the experiments by Pincus and Elmadjan[24] that the lymphocytopenia of acute stress does not attain such low values as those found in the patients with heart disease. The relation of emotional stress to the white blood cell picture is, moreover, complicated by the finding of Farris[16] that emotion by itself causes lymphocytosis. Also, many low lymphocyte counts were found in our patients to occur only after the disease had lasted several days or weeks, when an acute stress situation would no longer exist or would have passed its peak. However, this stress factor deserves further investigation, especially in view of the role of the pituitary gland (Colfer and associates[8]) and the suprarenal cortex in regulating the number of lymphocytes (White and Dougherty[32]), even if at present no direct relation can be seen in our cases.

That circulatory factors have an influence on the white blood cell picture has been previously contended (Rückel and Spitta;[27] Ellermann and Erlandsen[12]). The main factor would be a slowing of the blood stream and stagnation of the white blood cells in the capillary bed. However, this would not explain the selective lymphocytopenia and the frequent relative and absolute neutrophilia. In this uncertainty about the pathogenesis of lymphocytopenia hitherto unknown factors cannot be ruled out. Future work will not only have to attempt to explain the pathogenesis, but to show also whether marked lymphocytopenia is of diagnostic and prognostic value.

In the present report I have tried not to give the impression that lymphocyte counts below 1,000 per cubic millimeter occur only in diseases of the heart, although it may be that when they are found in other conditions circulatory insufficiency is a factor in their production.

SUMMARY

Hospital charts of patients with coronary infarction were examined with a view to determining the lymphocyte counts in these cases. A relatively large number had lymphocyte counts under 1,000 per cubic millimeter, counts which were not found in normal persons. Patients of Altana and Pulino[2] seem to have shown similar blood reactions. Marked lymphocytopenia was also found in patients with rheumatic heart lesions and with hypertension but less frequently than in those with coronary infarction. Lymphocytopenia was present in a moderate number of old people hospitalized for hernia operations. The pathogenesis and clinical importance of marked lymphocytopenia are briefly discussed.

REFERENCES

1. Aberg, M. L., and Tötterman, G.: Om den vita blodbilden hos adringar, Nord. med. **13**:39, 1942.
2. Altana, G., and Pulino, C.: Il quadro leucocitario nello scompenso cardiaco, Folia cardiol. **6**:193, 1947.
3. Altschul, R.: White Blood Cells in Old Age and in Arteriosclerosis, Circulation **2**:470, 1950.
4. Augarten, M.: Ueber die Variabilitaet des normalen weissen Blutbildes, Thesis, Hamburg, 1938, H. Schimkes.
5. Boerner, F.: Standard Normals and Normal Ranges in Hematology, Am. J. Clin. Path. **1**:391, 1931.
6. Branscheid, F., and Ehrhardt, L.: Die Lymphocytenzahlen des Gesunden in Jena, Klin. Wchnschr. **18**:1293, 1939.
7. Castelle-Rothe, A.: Erhoehung der relativen Lymphozytenwerte beim Gesunden und Kranken als periodische Erscheinung, Folia haemat. **65**:239, 1941.
8. Colfer, H. F., de Groot, J., and Harris, G. W.: Pituitary Gland and Blood Lymphocytes, J. Physiol. **111**:328, 1950.
9. Corell, M.: Das normale Blutbild beim Greise, Thesis, Abstr. Anat. Bericht. **18**:265, 1926.
10. De la Balze, F. A., Reifenstein, E. C., Jr., and Fuller, Albright: Differential Blood Counts in Certain Adrenal Cortical Disorders, J. Clin. Endocrinol. **6**:312, 1946.
11. Downey, H.: Handbook of Hematology, New York, 1938, Paul B. Hoeber, Inc.
12. Ellermann and Erlandsen: Quoted by Augarten.[4]
13. Elmadjan, F., Freeman, H., and Pincus, G.: The Adrenal Cortex and the Lymphocytopenia Due to Glucose Administration, Endocrinology **39**:293, 1946.
14. Elmadjan, F., and Pincus, G.: The Adrenal Cortex and the Lymphocytopenia of Stress, Endocrinology **37**:47, 1945.
15. Elmadjan, F., and Pincus, G.: A Study of the Diurnal Variation in Circulating Lymphocytes in Normal and Psychotic Subjects, J. Clin. Endocrinol. **6**:287, 1946.
16. Farris, E. J.: Increase in Lymphocytes in Healthy Persons Under Certain Emotional States, Am. J. Anat. **63**:297, 1938.
17. Freeman, H., and Elmadjan, F.: The Relationship Between Blood Sugar and Lymphocyte Levels in Normal Individuals, J. Clin. Endocrinol. **6**:668, 1946.
18. Hirschfeld, H., and Hitmair, A.: Handbuch der allgemeinen Haematologie, Berlin, 1938, Urban & Schwarzenberg.
19. Kracke, R. R.: Diseases of the Blood, Philadelphia, 1941, J. B. Lippincott Company.
20. Lazarus, S. S., Volk, B. W., Jacobi, M., and Zymaris, M.: Lymphocytic Response of Normal Individuals to Transient Hyper- and Hypoglycemia, Proc. Soc. Exper. Biol. & Med. **74**:432, 1950.
21. Marks, P. A., Marks, D. T., and Jailer, J. W.: Depression of Lymphocyte Counts After Orally Administered Glucose, J. Clin. Endocrinol. **8**:621, 1948.
22. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, 1931, Julius Springer.
23. Osgood, E. E., and Ashworth, C. M.: Atlas of Hematology, San Francisco, 1937, J. W. Stacey, Inc.
24. Pincus, F., and Elmadjan, F.: The Lymphocyte Response to Heat Stress in Normal and Psychotic Subjects, J. Clin. Endocrinol. **6**:295, 1946.
25. Reich, C., and Reich, E.: A Study of a Lymphocytic Hemogram, Am. J. M. Sc. **186**:278, 1933.
26. Rosenthal, N.: Hematological Aspects of Agranulocytosis, Am. J. Clin. Path. **1**:7, 1931.
27. Rückel and Spitta: Quoted by Müller, E. F., in Hirschfeld and Hitmair, Vol. 1, part 2.[18]
28. Schilling, V.: Das Blutbild und seine klinische Verwertung, ed. 9-10, Jena, 1933, Gustav Fischer.
29. Stieglitz, E. J.: Geriatric Medicine, Philadelphia, 1943, W. B. Saunders Company.
30. Vallastro, S.: Gli elementi morfologici del sangue, Haematologica **25**:579, 1943.
31. Weidenreich, F.: Quoted by Brodersen, J., in Möllendorff's Handbuch der mikroskopischen Anatomie II, Berlin, 1927, Julius Springer, p. 1.
32. White, A., and Dougherty, T. F.: Effect of Prolonged Stimulation of Adrenal Cortex, Endocrinology **36**:16, 1945.
33. Wintrobe, M. M.: Clinical Hematology, Philadelphia, 1947, Lea & Febiger.

SYSTOLIC AND DIASTOLIC LOADING OF THE HEART. I.

Physiologic and Clinical Data

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INTRODUCTION

SINCE Blix's studies[6] we know that the initial length of a muscle fiber may modify the energy of contraction and, consequently, the work done by such a fiber. This phenomenon so defines a length-tension or length-work curve both for an isolated muscle or for a single muscle fiber.[43] The curve first rises, then falls, with an intermediate maximum point; in other words, there is an optimum length for the muscle to develop the maximum of contractile energy.

The same phenomenon applies to the heart.[42] The initial length may then be modified by modifying the diastolic filling while the work can be approximately calculated by multiplying the output by the mean pressure developed by the heart. The new curve shows a certain diastolic filling which permits a maximal work to be done. From the beginning to the top of the curve there are favorable conditions for the adaptation of the heart, which can increase the work done as the diastolic filling increases. In this case the loading of the heart primarily modifies its diastolic conditions, so we speak of "diastolic overloading."

When the heart is under hemodynamic conditions which abnormally increase the diastolic filling (as in the case of regurgitation of any heart valve), the effect of Starling's law is easily understood: the chamber that is overloaded develops a stronger contraction, increases its systolic stroke, and so compensates totally or in part the effects of valvular regurgitation. The problem would be a little more complicated when the hemodynamic abnormality, without altering by itself the diastolic filling, primarily modifies the systolic action of the heart, that is, the conditions present once the heart is in the middle of its contraction. This is the case in arterial hypertension, aortic stenosis, etc. At present, it is admitted[17,20-23,28,30,36,52,53] that even in these cases the heart compensates by means of Starling's mechanism, only not immediately, with the first beats after the installation of the obstacle. For a few beats the heart would fail to empty as before, so increasing with this remnant the diastolic filling, which in turn would make Starling's mechanism act. This opinion is sustained by the results of acute experiments* on the heart-lung preparation.[42] In consequence it is agreed that Starling's law is the fundamental mechanism of compensation both for overloadings which are primarily systolic or diastolic; the cardiologist does not try to make an essential distinction between these two types of overloadings.

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*We agree with Moe and associates' objection[40] in the sense that Patterson and associates were actually measuring the increments of coronary flow as part of the increments of heart volume.

DISCUSSION

A. *Work of a Muscle Which Is "After-loaded"*.—If the initial or diastolic length of a muscle is kept constant as the loads are varied, we say that it has variable "after-loading" or "systolic loading," since the mechanical diastolic conditions are the same while those during contraction have been modified. Under these circumstances a progressive increase of load determines the amount of work, which increases at first, then declines.[19] The general form of the curve is similar to that of Starling's phenomenon only its peak is anticipated and less high. At any rate, there also exists an interval (first limb of the curve) where the muscle may perform increasing work as the load increases. This phenomenon has also been found in cardiac muscle.[45] Let us indicate that not only the work but the total oxygen consumption,[26] and probably the cardiac efficiency as well, show an initial increase for increasing loads.[19,22] In the case of an innervated heart, the systolic overloadings due to elevation of the aortic pressure produce some bradycardia, thus giving rise to a still higher cardiac efficiency.[34]

In considering these facts we see that, even if one accepts that Starling's law may act as a compensatory mechanism in the case of a systolic overloading, *the increments in the work of the heart are due in a considerable proportion to mechanisms which are independent of the initial length of the fibers.* Nevertheless, as the work is approximately equal to the mass of blood ejected times the mean pressure developed, this product could increase even when the systolic output diminishes, provided the rate of increase for the systolic loading was higher than the rate of decrease for the systolic output. This leads us to consider the length-tension curves of isolated muscle or the volume-pressure curves of the heart.

B. *The Length-Tension Curve of a Muscle in Diastole and Systole.*—For a relaxed muscle the slope of the curve is steeper as the length increases, while in a contracted muscle the curve is almost vertical at first, then its slope diminishes until it practically disappears[6] (Fig. 1). This is also true for the volume-pressure curve of the heart[42] (Fig. 1). A line uniting the first (diastolic) curve to the second (systolic) curve represents the different lengths and tensions developed during mechanical activation of the muscle. A line going vertically from the first to the second curve represents the tension changes in an isometric contraction (in this way the length remains constant). A line going horizontally from the first to the second curve represents the length changes in an isotonic contraction (now the tension remains constant). Actually, neither an isolated muscle nor the heart contract in a simple isometric or isotonic form but they pass from the first to the second curve, following a peculiar trajectory which is at first almost isometric then almost isotonic.

By the consideration of these curves it is to be expected that, if there is no compensatory mechanism which could develop once the muscular contraction starts,* an increase in the *systolic loading* would prolong the "isometric" phase of contraction and reduce the amount of shortening during the "isotonic" phase.

*This is actually the hypothesis assumed by the cardiologists who have discussed the problem.

The difference between this amount of shortening and that developed with a smaller systolic loading would be the cause of the systolic remnant of blood in the case of the heart. This remnant in turn would be the cause of an increased diastolic filling during the next contraction, thereby putting into play Starling's compensatory mechanism. But, at least for a considerable interval, the increment of diastolic filling so produced would be relatively small compared to the increment of work and even compared to the increment of systolic load, because of the lesser slope of the diastolic length-tension curve as compared to that of the systolic one (Fig. 1). In turn, a *diastolic overloading* would produce an increment of work which is in percentage strictly equal to the increment of diastolic loading.

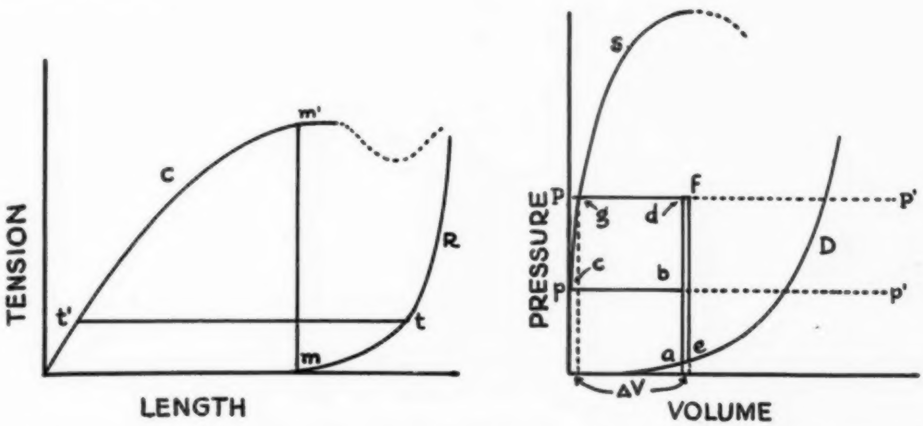

Fig. 1.—In the length-tension diagram: *R*, curve of a relaxed muscle; *C*, curve of a contracted muscle; *m m'*, isometric contraction; *t t'*, isotonic contraction.

In the volume-pressure diagram: *D*, diastolic curve; *S*, systolic curve; *a b c*, theoretical contraction for a certain (p') afterloading; *a b d g*, first theoretical contraction for a higher (P') afterloading; *e f g*, second theoretical contraction for a higher (P') afterloading.

Compare the increment in the diastolic volume ($\triangle V$) with the increment in the work (surface of the parallelogram *e f g* minus surface of the parallelogram *a b c*). From Patterson et al.[42]

The mere consideration of these facts should make us expect, in systolic overloading, a mechanism of compensation, an oxygen consumption and metabolic circumstances greatly differing from those present in diastolic overloading, even if the percentage of such overloading were the same in both cases. Furthermore, it is known that the amount of energy liberated by a muscle does change even if the loading conditions were modified once the muscular contraction has started.[19,26] On the other hand, a higher work and higher oxygen consumption induce muscular hypertrophy, thus permitting a greater amount of shortening for equal systolic loading and rendering unnecessary the previous fiber lengthening which was supposed to maintain unaltered the output.

Consequently, we feel justified in postulating, as a working hypothesis, the idea of a dualistic behavior of the heart in the presence of diastolic or systolic overloadings, in order to examine the clinical facts and see whether or not this hypothesis is tenable and of practical use.

C. *The Different Types of Clinical Ventricular Overloadings.*—Let us classify the ventricular overloadings in four groups: diastolic overloading (D.O.), systolic overloading (S.O.), composite overloading upon a single ventricle (C.O.) or variable overloading for a single ventricle (V.O.).

1. *Diastolic overloadings (D.O.).*—The right ventricle (R.V.) may face a D.O. in the case of pulmonary regurgitation, tricuspid regurgitation, auricular septal defect with left-to-right shunt, anomalous pulmonary veins draining into the right auricle or the superior vena cava, etc. The left ventricle (L.V.) may have a D.O. in the case of aortic regurgitation, mitral regurgitation, patent ductus arteriosus with aortopulmonic shunt, auricular septal defect with right-to-left shunt, etc.

Both ventricles may show an equal degree of D.O. in the case of an arteriovenous aneurism.

2. *Systolic overloadings (S.O.).*—The R.V. may have S.O. in the case of pulmonary stenosis or in pulmonary hypertension as is found in mitral stenosis, chronic cor pulmonale, certain cases of patent ductus arteriosus, etc. The L.V. will be in S.O. in the case of aortic stenosis, arterial hypertension, etc.

3. *Composite overloadings (C.O.) upon a single ventricle.*—The R.V. may have both D.O. and S.O. in Fallot's tetralogy (the pulmonary stenosis together with the overriding of the aorta determine the S.O. while the blood shunted from the R.V. to the aorta increases the diastolic loading of the right cavities); in Fallot's trilogy (pulmonary stenosis, interauricular communication, and intact interventricular septum) when the shunt from the left auricle to the right auricle persists; in Lutembacher's syndrome; in mitral stenosis associated with tricuspid insufficiency or pulmonary regurgitation; in patent ductus arteriosus associated with a shunt from the pulmonary artery to the aorta or with pulmonary regurgitation; in acute cor pulmonale, where by definition the sudden increase of pulmonary pressure forces the R.V. and hinders its complete emptying, etc.

The L.V. is under a C.O. in the case of a double aortic lesion, an aortic stenosis associated with mitral regurgitation, an arterial hypertension associated with aortic regurgitation, or with mitral regurgitation, a patent ductus arteriosus combined with coarctation of the aorta of the "adult" type, etc.

4. *Variable overloadings (V.O.) for a single ventricle.*—

a. Diastolic overloadings becoming systolic: The ligation of a patent ductus arteriosus or that of an arteriovenous aneurism produces at the same time a decrease in the diastolic filling of the L.V. and an increase in the mean pressure of the aorta (so a S.O. of the L.V.).

b. Systolic overloadings becoming diastolic: An imperfect example of this type is found in the R.V. when a mitral stenosis with marked pulmonary hypertension develops a functional tricuspid insufficiency, so giving rise to a lowering of the pulmonary pressure with higher diastolic filling of the R.V.[10,17,22,36,52]

c. Systolic overloadings becoming composite: When a S.O. of the R.V. is of very high magnitude or sudden onset or it becomes complicated by myocarditis, an incomplete emptying of the R.V. (a D.O. of the R.V.) is produced.[4b] This is the case in long-standing and high pulmonary hypertension, in marked pulmonary stenosis, in mitral stenosis complicated by acute rheumatic carditis, etc.

A progressively increasing pulmonary hypertension complicating a patent ductus arteriosus may induce a shunt from the pulmonary artery to the aorta, by these means the S.O. of the R. V. becoming a C.O.[16,31,37]

Once a coronary insufficiency or a myocarditis develops in the case of aortic stenosis, coarctation of the aorta, or arterial hypertension, the L.V. fails and the initial S.O. is converted into a C.O.

D. *Clinical, Radiologic, and Pathologic Evidence.*—

1. *Cases with S.O.*—Experience shows that systolic overloadings of the L.V. leave the heart volume within normal limits for a long time, merely inducing a shortening of the radius of curvature of the L.V. as shown by x-ray examination.[20-23,36,39,44,47] In these cases, autopsy shows a thick-walled L.V. without

important dilatation of its cavity.[39] There may even be a slight diminution in the size of the cavity.[51] During the first stages of arterial hypertension, angiocardiography is not only unable to discover an incomplete emptying of the L.V. but the so-called "systolic images" of the L.V. (where the left auricle and the aorta appear filled while the left ventricular cavity is not shown) are still more frequent than in normal subjects.[13] It is only when the S.O. of the L.V. is associated with a poor myocardial condition,[20,21,22,36,39,44,47,52] that heart failure and dilatation of the L.V. supervene, according to clinical, x-ray, angiocardiographic, and pathologic evidence.

Systolic overloading of the R.V. determines an incomplete emptying more readily than that of the L.V., probably due to the interaction of three factors: (1) it attains magnitudes proportionally higher (the mean pressure of the aorta rarely approaches a 170 per cent of the normal value, while that of the pulmonary artery may reach a 500 or even 600 per cent of it); (2) the R.V. has a thinner wall; and (3) a great number of cases with pulmonary hypertension (those due to mitral stenosis) are accompanied by severe, diffuse myocardial damage. This leads the R.V. to an anatomic behavior which is not so characteristic as that of the L.V. Nevertheless, in cases with S.O., one can find a R.V. with a thickening of the free wall and a slight or moderate dilatation of the outflow tract only.[3,11] The difficulty in making evident an x-ray enlargement of the R.V. during the first stages of a well-compensated mitral stenosis, a moderate pulmonary stenosis, a patent ductus arteriosus, or a chronic cor pulmonale is also well known.[3,11,22,36,44,47] One can even find at autopsy a thickening of the wall with diminution of the cavity of the R.V. in spite of S.O., especially if there is a condition hindering the diastolic filling. We have seen such a case at the Instituto de Cardiologia de México. (V.B.L., 17100; 4½-year-old boy with marked cyanosis. Angiocardiography and autopsy proved a pulmonary stenosis with interauricular communication giving rise to right-to-left shunt.) Taussig reports[49] two more cases: one, a tetralogy of Fallot with extreme pulmonary stenosis and a patent foramen ovale which "would have permitted some flow of blood from the right auricle to the left," in which the cavity of the R.V. was found to be "extremely small"; the other, also a tetralogy of Fallot with slight dextroposition of the aorta and marked pulmonary stenosis, in which "the R.V. was a small, thick-walled chamber."

However, a C.O. easily supervenes once a tricuspid or pulmonary regurgitation or a right ventricular failure complicates the S.O. of the R.V.

2. *Cases with D.O.*—D.O. of the L.V. usually induces a considerable dilatation of the cavity with slight thickening of the wall. The former appears early at clinical and x-ray studies and is not necessarily related to the degree of left ventricular failure.[1,22,36,44,47,52] Cardiologists are well acquainted with such a "paradox" as that of a dilated L.V. with adequate myocardial sufficiency in cases of aortic regurgitation[1] or patent ductus arteriosus.[41] Furthermore, a dilatation of the L.V. after Blalock-Taussig[4a,5,7,35] or a Brock[8] operation (both surgical procedures increase the blood return to the L.V.), without evidence of left ventricular failure, is a well-proved fact.

In D.O. of the R.V. one can find the most outstanding dilatations of the R.V., often associated with dilatation of the right auricle. Such dilatations usually affect both tracts of the ventricular cavity (in contrast to the simple dilatation of the outflow tract as seen in S.O.), a preponderence of the inflow tract not being rare. These findings have been abundantly mentioned in tricuspid insufficiency,[2,17,22,24,48] interauricular septal defect,[14,17,22,24,36,44,49,52] old mitral stenosis with rheumatic carditis, acute cor pulmonale,[27,33,38,54] anomalous drainage of the pulmonary veins into the right auricle or the superior vena cava, etc.[12,15,18,25,29,46,49,50]

Among interauricular communications one can also see the "paradox" of dilated right ventricular cavities without right ventricular insufficiency. The total reduction of heart enlargement after the ligation of an arteriovenous aneurysm (producing disappearance of the D.O. for the whole heart) is also a well-known fact.[9,17,22,24,36,44,47,52]

We feel that any cardiologist with a fair practice can easily confirm and enlarge the number of examples proving a dualistic behavior of the ventricles under systolic or diastolic overloadings and, in turn, can benefit in his practice by keeping this viewpoint in mind.

CONCLUSIONS

A. *Cases Where Starling's Mechanism Comes Into Play.*—The mediation of Starling's mechanism in a case of primitive D.O. seems out of the question. It may act by itself or be aided by a moderate tachycardia which permits an increase of the cardiac output without importantly increasing the stroke volume, so allowing an important reserve in the utilization of Starling's law. Under these circumstances, the higher total oxygen consumption of the muscle fibers induces a ventricular hypertrophy, giving rise to a widening of that interval in which an increase of diastolic filling determines an increase of heart work. For these cases with a primitive D.O., it is doubtful that a ventricular dilatation could be interpreted as a failure of the ventricle.

On the other hand, the probability for Starling's mechanism to act in cases of primitive S.O. increases only as the functional capacity of the myocardium is decreased or the magnitude of the loading increases. Consequently, for these latter cases one may accept the opinion that ventricular dilatation is to be considered as an evidence of myocardial failure.

B. *Cases Where Mediation of Starling's Law Is of Unimportant Account.*—This seems to be the case for S.O. of moderate degree with a healthy myocardium. The probabilities of, and the span of time for this being the case, are higher for the left ventricle. It is doubtful whether a clinical S.O. requires Starling's compensatory mechanism during the first moments after its installation,* as clinical cases with a healthy myocardium can hardly be compared with a decaying heart-lung preparation in which the loading is applied suddenly. But even if one accepts its mediation during these first moments it seems completely void of importance once the cardiologist confronts the case with a well-compensated heart.

*Arterial hypertension acting upon an innervated heart is a particular case, as it can slow down the rate, so increasing its diastolic filling in a way which has nothing to do with the classically accepted incomplete emptying of the heart. However, this change of rate does set into action Starling's mechanism.

SUMMARY

1. The authors briefly present the unicist classical theory which considers Starling's mechanism as a compensatory mediator both for primarily diastolic and for primarily systolic overloadings.

2. The theoretical possibilities that Starling's mechanism could be of no important value for primarily systolic overloadings are presented.

3. A brief review is made of clinical, x-ray, and autopsy evidence in favor of this theoretical viewpoint.

4. It is concluded that the theory of a dualistic compensatory mechanism of a heart which confronts a diastolic overloading or a systolic one is of great advantage over the unicist theory which reduces both to Starling's law.

5. The authors will show in a paper to follow that it is also possible to discover a different electrocardiographic behavior for different types of overloadings.

REFERENCES

1. Aceves, P. S. (Hospital Section, Inst. Nac. Cardiol. México.): Personal communication.
2. Aceves, P. S., and Carral, R.: The Diagnosis of Tricuspid Valve Disease, Am. Heart J. **34**:130, 1947.
3. Aschoff, L.: Tratado de Anatomía Patológica, Vol. II, Madrid, 1934, Edit. Labor.
4a. Baker, Ch., Brock, R. C., Campbell, M., and Suzman, S.: Morbus Coeruleus. A Study of 50 Cases After the Blalock-Taussig Operation, Brit. Heart J. **11**:170, 1949.
4b. Bing, R. J., Heimbecker, R., and Falholt, W.: An Estimation of the Residual Volume of Blood in the Right Ventricle of Normal and Diseased Human Hearts in Vivo, Am. Heart J. **42**:483, 1951.
5. Blalock, A., and Taussig, H.: The Surgical Treatment of Malformations of the Heart. Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. **28**:189, 1945.
6. Blix: Skand. Arch. f. Physiol. **5**:150, 1895. Mentioned by Patterson et al. in J. Physiol. **48**:465, 1914.
7. Bozal Urzoy, V., and Nerin Mora, E.: Tetralogy of Fallot. Analysis of 41 Cases of Patients Treated Surgically at U. of Minnesota, J. Pediat. **35**:401-411, 1949.
8. Brock, R. C., and Campbell, M.: Infundibular Resection or Dilatation for Infundibular Stenosis, Brit. Heart J. **12**:403, 1950.
9. Cabrera C., E., and Monroy, J. R.: Reprecusión de la hemodinámica sobre el electrocardiograma en un caso de fístula arteriovenosa, Arch. inst. cardiol. México **21**:457, 1951.
10. Cesarman, T. E., and Mendoza, C. M.: Unpublished papers.
11. Costero, I. (Department of Pathology, Inst. Cardiol. México): Unpublished data.
12. Cournand, A.: Cardiac Catheterization, New York, 1949, Commonwealth Fund.
13. Dorbecker C., N. (Department of Radiology, Inst. Cardiol. México): Personal communication.
14. Dorbecker C., N., and Deschamps, J.: Cavidades derechas y angiocardiografía, Arch. inst. cardiol. México **19**:187, 1949.
15. Dotter, C. T., Hardisty, N. M., and Steinberg, I.: Anomalous Right Pulmonary Vein Entering Inferior Vena Cava; 2 Cases Diagnosed During Life, Am. J. Med. Sc. **218**:31-36, 1949.
16. Douglas, J. M., Burchell, H. B., Edward, J. E., and Dry, T. S.: Systemic Right Ventricle in Patent Ductus Arteriosus; Report of a Case With Obstructive Pulmonary Vascular Lesion, Proc. Staff Meet., Mayo Clin. **22**:413, 1947.
17. Dressler, W.: Clinical Cardiology, New York, 1942, Paul B. Hoeber, Inc.
18. Edward, J. E., Du Shane, J. W., Alcott, D. L., and Burchell, H. B.: Thoracic Venous Anomalies. III. Atresia of the Common Pulmonary Vein, the Pulmonary Veins Draining Wholly Into the Superior Vena Cava, Arch. Path. **51**:446, 1951.
19. Fenn, W. O.: A Quantitative Comparison Between the Energy Liberated and Work Performed by the Isolated Sartorius Muscle of the Frog, J. Physiol. **58**:175, 1923.
20. Fishberg, A.: Hypertension and Nephritis, Philadelphia, 1944, Lea & Febiger.
21. Fishberg, A.: Heart Failure, Philadelphia, 1948, Lea & Febiger.
22. Friedberg, K. Ch.: Diseases of the Heart, Philadelphia, 1949, W. B. Saunders Company.
23. Glasser, O.: Medical Physics, Vol. II, Chicago, 1950, The Year Book Publishers, Inc.
24. Goldberger, E.: Heart Disease, Its Diagnosis and Treatment, Philadelphia, 1951, Lea & Febiger.

25. Grishman, A., Poppe, I. M. H., Simpson, R. S., and Suzman, M. L.: Roentgenographic and Angiocardiographic Aspects of Abnormal Insertion of Pulmonary Veins, Am. J. Roentgenol. **62**:500-508, 1949.
26. Hill, A. V.: Proc. Roy. Soc., London, s. B. **126**:136, 1938. Mentioned by Fenn, W. O.: Physical Chemistry of Cells and Tissues, Philadelphia, 1945, The Blakiston Co.
27. Horn, H., Dack, S., and Friedberg, K. Ch.: Cardiac Sequelae of Embolism of the Pulmonary Artery, Arch. Int. Med. **64**:296, 1939.
28. Houssay, B. A.: Human Physiology, New York, 1951, McGraw-Hill Book Company.
29. Howald, E.: A Case of Congenital Anomaly of the Heart With Abnormal Drainage of the Pulmonary Veins, Helvet. paediat. acta. **4**:322, 1949.
30. Howell, W. H.: A Text Book of Physiology, Philadelphia, 1940, W. B. Saunders Company.
31. Johnson, R., Wermer, P., Kruchner, M., and Cournand, A.: Intermittent Reversal of Flow in a Case of Patent Ductus Arteriosus, Circulation **1**:1293, 1950.
32. Kiese, K., and Garan, R. S.: Mechanische Leistung, Grösse und Sauerstoffverbrauch des Warmblüterherzens, Arch. f. exper. Path. u. Pharmakol. **188**:226, 1938.
33. Krumbhaar, E. B.: Note on Electrocardiographic Changes Accompanying Acutely Increased Pressure Following Pulmonary Artery Ligature, Am. J. Med. Sc. **187**:792, 1934.
34. Landowe, M., and Katz, L. N.: Circulatory System: Heart; Work and Failure. In Medical Physics, Vol. II, Chicago, 1950, The Year Book Publishers, Inc.
35. Leininger, C. R.: Congenital Pulmonary Stenosis; Post-operative Observations on 214 Children, Am. J. Dis. Child. **81**:465, 1951.
36. Lemierre, A.: Traité de Médecine, Tome X, Paris, 1948, Masson et Cie.
37. Limon, L. R., Bouchard, F., Rubio Alvarez, V., Cahen, P., and Novelo, S.: El cateterismo intracardiaco. III. Persistencia del conducto arterioso con hallazgos, clínicos atípicos. Presentación de 8 casos, 5 de los cuales tenían cianosis. Pruebas de la existencia de "shunt" invertido y cruzado, Arch. inst. cardiol. México **20**:147, 1950.
38. Love, W. S., Brugler, G. W., and Winslow, N.: Electrocardiographic Studies in Clinical and Experimental Pulmonary Embolization, Ann. Int. Med. **11**:2109, 1938.
39. Master, A. M.: The Electrocardiogram and X-ray Configuration of the Heart, Philadelphia, 1942, Lea & Febiger.
40. Moe, G. K., Wood, E. H., and Vischer, M. B.: Aortic Pressure and Diastolic Volume Law of Energy Output in Cardiac Contraction, Proc. Soc. Exper. Biol. & Med. **40**:460, 1939.
41. Novelo, S. (Department of Congenital Heart Diseases, Inst. Cardiol. México): Personal communication.
42. Patterson, S. W., Piper, H., and Starling, E. H.: The Regulation of the Heart Beat, J. Physiol. **48**:465, 1914.
43. Ramsey, R. W., and Street, S. F.: Isometric Length-Tension Diagram of Isolated Skeletal Muscle Fibers of the Frog, J. Cell. & Comp. Physiol. **15**:11, 1940.
44. Roesler, H.: Clinical Roentgenology of the Cardiovascular System, Springfield, Ill., 1943, Charles C Thomas, Publisher.
45. Rosenblueth, A., and Maling, H.: Unpublished papers.
46. Sanes, S.: Anomalous Drainage of Pulmonary Veins Into Coronary Sinus, Am. J. Dis. Child. **58**:354-361, 1939.
47. Schwedel, J. B.: Ann. of Roentgenology, Vol. 18. Clinical Roentgenology of the Heart, New York, 1950, Paul B. Hoeber, Inc.
48. Sodi Pallares, D., Bisteni, A., and Herrmann, G. R.: Some Views of the Significance of the qR and QR Type Complex in the Right Precordial Leads in the Absence of Myocardial Infarction, Am. Heart J. **43**:716, 1952.
49. Taussig, H. B.: Congenital Malformations of the Heart, New York, 1947, The Commonwealth Fund.
50. Vass, A., and Keller, Mc. J.: Drainage of Pulmonary Veins Into Coronary Sinus, Am. J. Dis. Child. **78**:906, 1949.
51. Velázquez, T.: Capacidad de las cavidades cardíacas en estado normal y patológico, Arch. inst. cardiol. México **20**:495, 1950.
52. White, P. D.: Heart Disease, New York, 1945, The MacMillan Medical Monographs.
53. Wiggers, C. J.: Physiology in Health and Disease, Philadelphia, 1934, Lea & Febiger.
54. Zuckermann, R., Rodriguez, M. I., Sodi Pallares, D., and Bisteni, A.: Electropathology of Acute Cor Pulmonale, Am. Heart J. **40**:805-824, 1950.

SYSTOLIC AND DIASTOLIC LOADING OF THE HEART. II.

Electrocardiographic Data

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THE ORIGINS of this paper can be found in the publications of the Department of Electrocardiography of the Institute of Cardiology of Mexico.* These publications have had two fundamental aims: (1) to give not merely a description but a true semeiologic interpretation of electrocardiograms, and (2) to elucidate the electrogenesis of them. On the other hand, we had arrived at the conviction that the clinical, x-ray and autopsy behavior of the ventricles is different in systolic or diastolic overloadings.[13] So we were led to investigate the different electrocardiographic behavior.

OVERLOADINGS OF THE RIGHT VENTRICLE

1. *Diastolic Overloading of Right Ventricle.*—We have observed that a primitive diastolic overloading of the right ventricle produces, frequently and early, a complete or incomplete right bundle branch block, as judged by right axis deviation and especially by the QRS aspect in V_1 with a double R, a polyphasic or just notched complex (Fig. 1). Sometimes, this pattern has to be looked for upon the right side of the chest.

Almost every case of interauricular communication with left-to-right shunt shows a right bundle branch block.[3,9,23,51,72] Among thirty-five cases of interauricular communication studied by Vizcaino and associates,[72] all but one (in this case the shunt was probably a right-to-left one) had a complete or incomplete right bundle branch block. In sixty-two cases reported by Barber and associates,[3] 95 per cent showed a right bundle branch block. On the contrary, in tricuspid atresia, where the auricular septal defect gives rise to a right-to-left shunt, a right bundle branch block is much less frequent. In consequence we believe that it is not the anatomic defect by itself but the hemodynamic changes which produce a right bundle branch block in interauricular communications.

In cases of tricuspid insufficiency proved at autopsy, a right bundle branch block is found in 47 per cent[12] or 65 per cent.[64] In cases of tricuspid insufficiency, we have often observed that both the signs of tricuspid regurgitation (liver pulsation and Rivero-Carvallo's murmur) and those of right bundle branch block diminish or disappear as the heart failure improves (Fig. 2).

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Among congenital heart diseases proved at autopsy,[77] those cases with right bundle branch block coincide with a dilated right ventricle (this can be taken as testimony of a primitive or secondary diastolic overloading of the right ventricle).

In Fallot's trilogy, where the left-to-right shunt between the auricles may disappear or even become inverted, a right bundle branch block is less frequent. Among fifteen cases, Joly and associates found only one case of right bundle branch block.[42] Among seven cases of marked pulmonary stenosis reported by Marquis[55] there was also only one case of right bundle branch block. In Fallot's tetralogy, the diastolic overloading of the right ventricle is frequent* and so is right bundle branch block, which can only be concealed by the signs of systolic

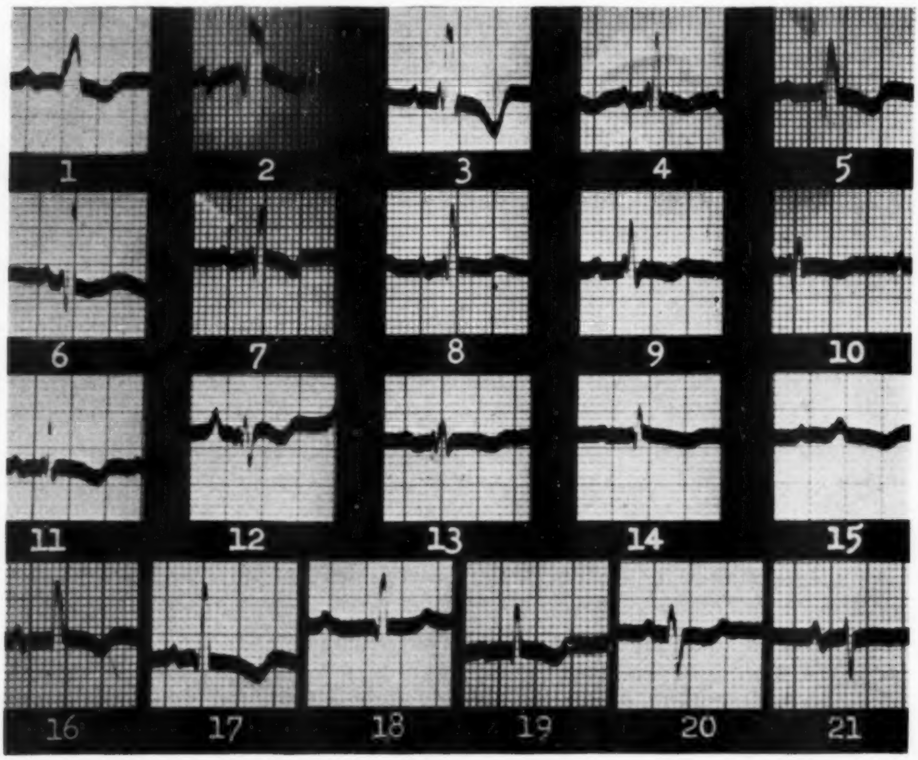


Fig. 1.—Lead V_1 in twenty-one cases of atrial septal defect proved by cardiac catheterization. Right bundle branch block is evident in the first nineteen cases, probable in Case 20 and absent in Case 21 (see text).

overloading of the right ventricle. As Zuckermann has shown,[77] right bundle branch block produces an early notching of the R wave at V_1 in these cases (Fig. 3). This notching can be seen in Zuckermann's cases[77] as well as in those of Donzelot and associates.[21] Acute cor pulmonale, which by definition produces a diastolic overloading of the right ventricle because it fails under the sudden pulmonary hypertension, frequently gives rise to incomplete right bundle branch block, which is often fleeting (Fig. 4). This has been proved in clinical practice[20,48,49,54,78] as well as in the experimental field.[24,25,47,53,79]

*The blood shunted from the right ventricle to the aorta goes through the systemic circulation and increases the venous return to the right cavities.

In the case of an aneurysm of the sinus of Valsalva opening into the right ventricle, an intraventricular block (probably a right bundle branch block) has frequently been reported.[38,59,68] In such cases the diastolic overloading of the right ventricle is obvious. But Snyder and Hunter[68] believe that the cause of the block is the extension of the aneurysm to the interventricular septum, so affecting the branches of the bundle of His. Espino and associates have reported a case where the right coronary artery opened directly into the right ventricle producing dilatation and a right bundle branch block[27] (Fig. 5).

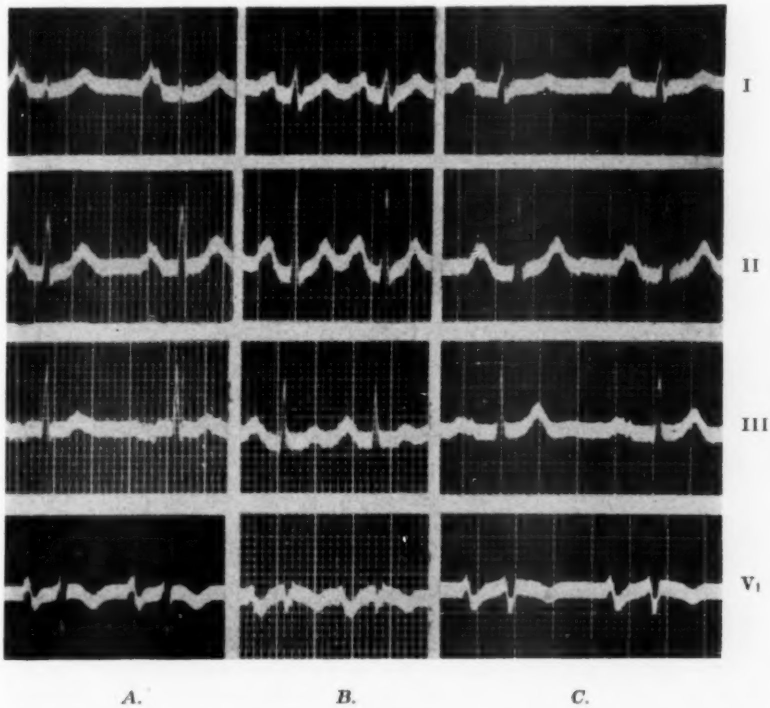


Fig. 2 (J.M.N., 12 yrs. old, Reg. 2263).—A case with mitral stenosis and regurgitation, and tricuspid regurgitation.

A, April 23. Patient had no evident signs of tricuspid regurgitation; incomplete right bundle branch block was absent.

B, April 25. Patient was in marked cardiac failure; tricuspid insufficiency is then identified for the first time and incomplete right bundle branch block appeared (notice the depth of S_1 and the notches of the QRS complex in V_1).

C, July 21. Cardiac failure had improved, tricuspid regurgitation and incomplete right bundle branch block no more evident.

When the pulmonary veins open into the superior vena cava or the right ventricle, a right bundle branch block has frequently been identified.[18,26,36,37,45,71] We have studied a case with pulmonary stenosis with one pulmonary vein draining into the superior vena cava, where a right bundle branch block was superimposed on the electrical signs of systolic overloading of the right ventricle (Fig. 6).

In a femoral arteriovenous fistula recently reported by us, there was an incomplete right bundle branch block which diminished with the manual compression of the fistula and after its surgical treatment[15] (Fig. 7).

It is interesting to notice that patent ductus arteriosus, which often overloads the right ventricle without increasing its diastolic filling, rarely produces a right bundle branch block. Only one case among twenty-one reported by Cabrera and associates[11] presented a right bundle branch block; here the catheterization of the right cavities showed a pulmonary regurgitation, leading to diastolic over-

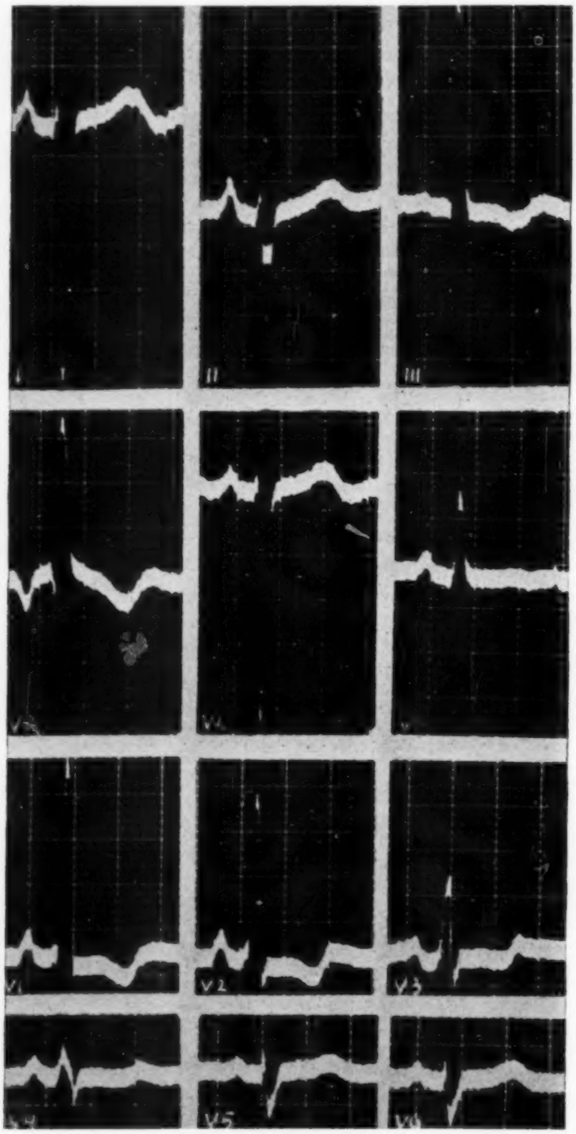


Fig. 3 (E.O., 9 yrs. old, Reg. 22055).—Fallot's tetralogy with interauricular communication proved at autopsy. Notice the high neat R wave preceded by an initial notch in V_1.

loading of the right ventricle. Johnson and associates[41] report a case, identical in all respects to ours. Douglas and associates[22] report a case of patent ductus arteriosus with right bundle branch block where there was a shunt from the pulmonary artery to the aorta, giving rise to a diastolic overloading of the right ventricle.

A systolic overloading of the right ventricle, eventually producing the failure of this ventricle, gives rise to its diastolic overloading. This happens in pulmonary hypertension (due to chronic pneumopathy or to mitral stenosis). In the former, the probability of a diastolic overloading of the right ventricle logically increases as the mean pressure of the pulmonary artery increases. Thus, the percentage of cases with electrical signs of right bundle branch block is higher as the mean pressure of the pulmonary artery increases.[40] In mitral stenosis, the probabilities of diastolic overloading of the right ventricle increase with the duration of the disease, as the myocarditis is more severe or when auricular

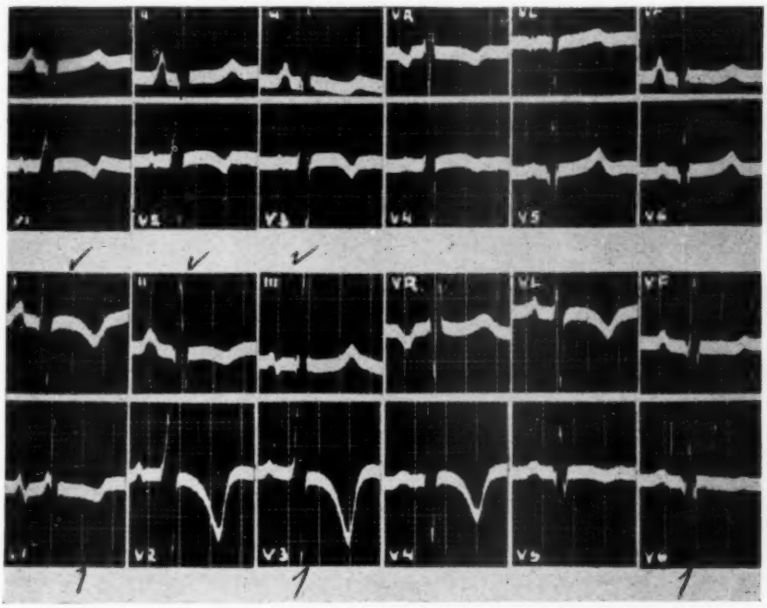


Fig. 4 (C.P.A., 17 yrs. old, Reg. 14349).—Upper row, Control tracing. Lower row, Tracing after pulmonary embolization. Notice the appearance of an incomplete right bundle branch block as well as an "ischemic" T wave in the right precordial leads.

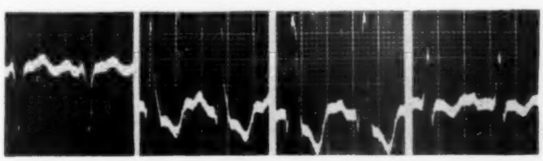


Fig. 5.—From left to right, Standard leads and V_1 in a case where the right coronary artery opened into the right ventricular cavity. Autopsy showed an important dilatation of this cavity. Notice a QRS complex in V_1 probably indicating right bundle branch block. Lead aV_R (not shown) had a late, slurred R wave.

fibrillation appears.[5,35] Thus, among autopsy cases with mitral stenosis (without anatomic evidence of tricuspid regurgitation) the percentage of incomplete right bundle branch block was 39 per cent.[12] On the other hand, among eighty clinical cases of "pure" mitral stenosis (those without systolic murmur and most of them without rheumatic activity), only thirteen cases had an incomplete right bundle branch block (most of these were above 40 years old and seven showed auricular fibrillation).[14]

Finally, it should be mentioned that in clinically normal subjects with incomplete right bundle branch block, the block usually diminishes or disappears with Valsalva's test (which diminishes the amount of blood returning to the right cavities), while it increases with Müller's test (which increases the amount of blood emptying into the right cavities)[75] (Fig. 8).

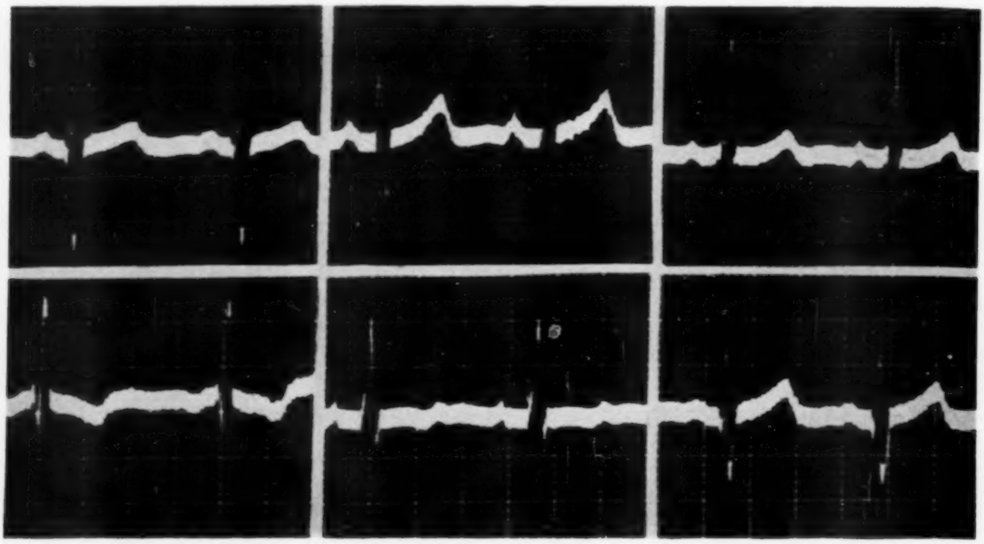


Fig. 6.—Upper row, Standard leads. Lower row, aV_R, V_1, V_6 (from left to right). Anomalous draining of a pulmonary vein into the superior vena cava and pulmonary stenosis, proved at cardiac catheterization. Notice the QRS complex in Lead I and the RsR complex in aV_R, indicating a probable incomplete right bundle branch block. At the same time, notice the high R wave with an initial slurring in V_1.

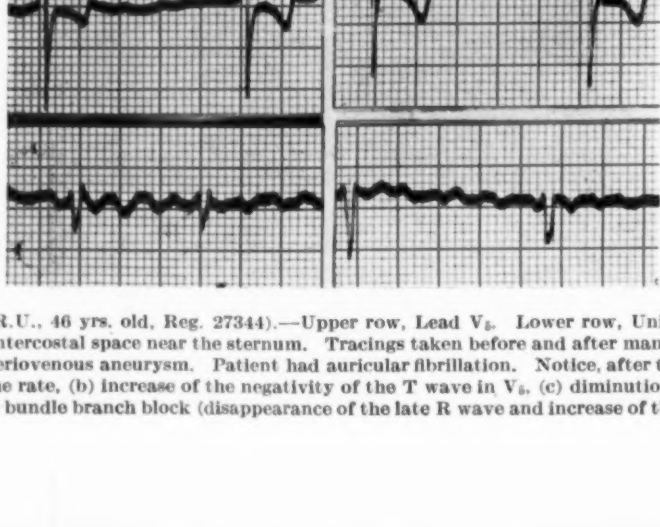


Fig. 7 (M.R.U., 46 yrs. old, Reg. 27344).—Upper row, Lead V_5. Lower row, Unipolar lead from the third right intercostal space near the sternum. Tracings taken before and after manual compression of a femoral arteriovenous aneurysm. Patient had auricular fibrillation. Notice, after the compression, (a) slowing of the rate, (b) increase of the negativity of the T wave in V_5, (c) diminution of the signs of incomplete right bundle branch block (disappearance of the late R wave and increase of the S wave).

2. *Systolic Overloading of Right Ventricle.*—We have observed that systolic overloading of the right ventricle increases the voltage of the R wave,[11,17,34,39,50,52,55] sometimes producing an initial slurring of it in V_1. If the systolic overloading is marked and of long duration, it can produce a negative T wave in V_1 (of the so-called "ischemic" type) (Fig. 9).* The QRS complex usually remains neat, of a monophasic (positive) or diphasic type (an RS, Rs, or qR complex), for a long time. The notched and polyphasic QRS complex appears only when the systolic overloading is complicated by diastolic overloading.

The electrocardiographic pattern of systolic overloading of the right ventricle can be seen in the cases of marked pulmonary stenosis reported by Marquis,[55] Brock and Campbell,[7,8] Zuckermann and associates,[77] and Coelho and associates.[17]

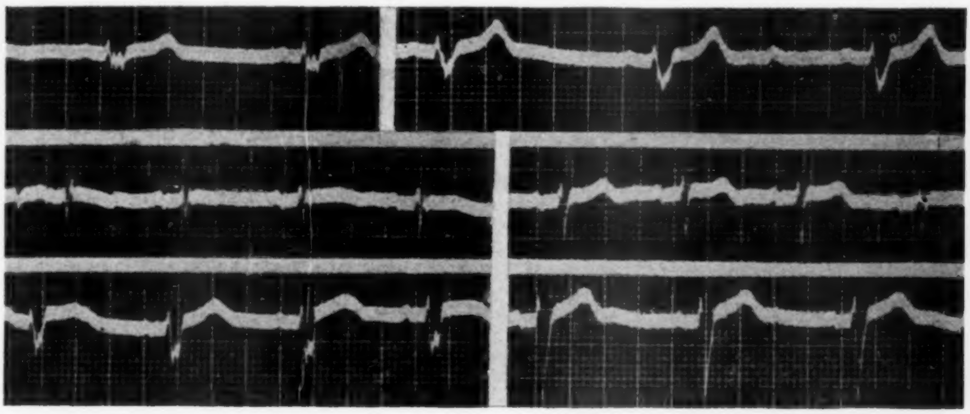


Fig. 8.—Lead V_1 in three cases with a normal heart showing an incomplete right bundle branch block before (left) and during (right) Valsalva's test. Notice that the notches of the QRS complex disappeared or diminished during the test.

In patent ductus arteriosus with high pulmonary pressure, a similar pattern is found (Fig. 10), but the negative "ischemic" T wave is rare.[11] Also we have found that in patent ductus arteriosus, the higher the pulmonary pressure, the higher the R wave in V_1.[11] In children with congenital heart disease, the quotient R/S in V_1 has been found to be greater the higher the pulmonary pressure.[34,50]

Among eighty cases of mitral stenosis (where pulmonary hypertension is usually of importance) we found high R waves in V_1 in seventeen cases.[14] It is possible that the lesser activity of the cardiopathy could avoid the development of a marked pulmonary hypertension. In 90 per cent of cases with Fallot's tetralogy, the R wave is equal or greater than the S wave in V_1.[21]

In chronic cor pulmonale[46,76] only 28 per cent of the cases show a high and delayed R wave (usually of the qR type) in V_1. The interpretation of this complex is a difficult one, as the heart has an abnormal position within the thorax. Some authors[31,46,60] believe this qR complex represents left ventricular potentials. Sodi[70] considers it as an incomplete right bundle branch block in most cases. Any way, a simple diphasic complex in V_1 is the rule in chronic cor pulmonale.

*Right axis deviation, which is the best sign of right ventricle hypertrophy, is equally produced by systolic overloading or diastolic overloading of the right ventricle.

OVERLOADINGS OF THE LEFT VENTRICLE

1. *Diastolic Overloading of Left Ventricle.*—In such cases one usually finds a high, delayed R wave in V_5 and V_6, with deep S waves in V_2 and V_3, and, especially, a high positive T wave in V_5 and V_6, without opposition between $\hat{A}_{QRS}$ and $\hat{A}_T$.

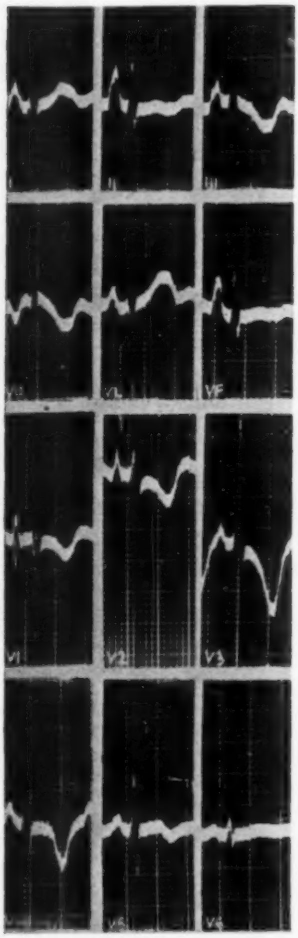


Fig. 9.

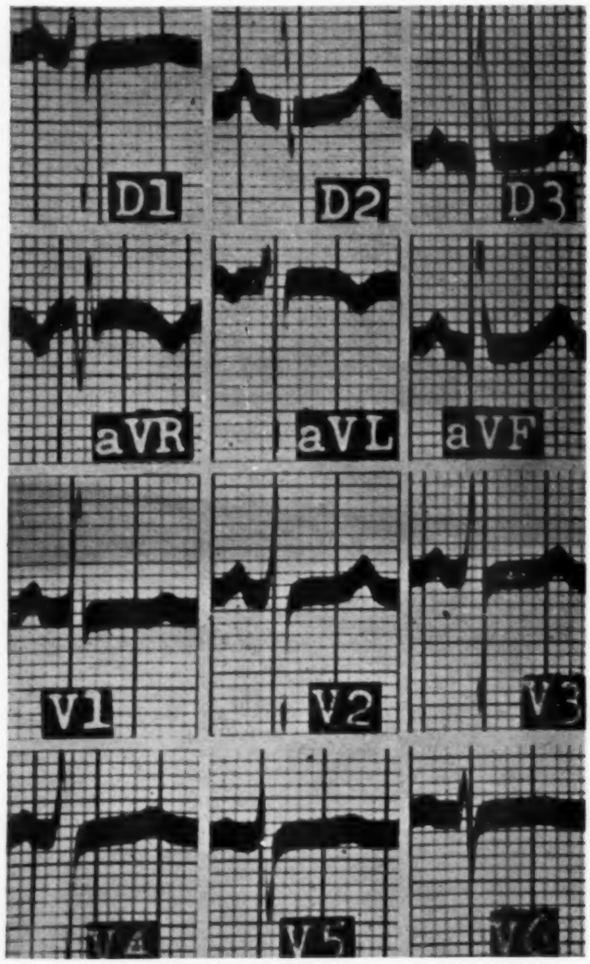


Fig. 10.

Fig. 9 (V.B.L., 4 yrs. old, Reg. 17100).—Pulmonary stenosis and interauricular communication proved at autopsy, giving rise probably to a double shunt. Notice (a) the high peaked P wave as it is found in cyanotic congenital cardiopathies, (b) an incomplete right bundle branch block (poliphasic complex in V_1, (c) a negative T wave of an "ischemic" type in the right precordial leads.

Fig. 10 (C.C.S., 16 yrs. old, Reg. 22678).—Patent ductus arteriosus proved at autopsy with marked pulmonary hypertension; cyanosis probably due to reversed shunt. Notice the rightward deviation of A_{QRS} and A_T and the high R wave with an initial slurring in V_1.

Among the cases of patent ductus arteriosus, we have found[11] that, in those leads transmitting the left ventricular potentials or "left ventricular leads," the R wave is high and the T wave is peaked, symmetrical, and of a voltage above the normal (Figs. 11 and 12,*A*). This was an unexpected finding, as it is usually accepted that left ventricular hypertrophy produces a secondary[10,19,39,69,74] or even a primary[74] negative T wave in those leads.

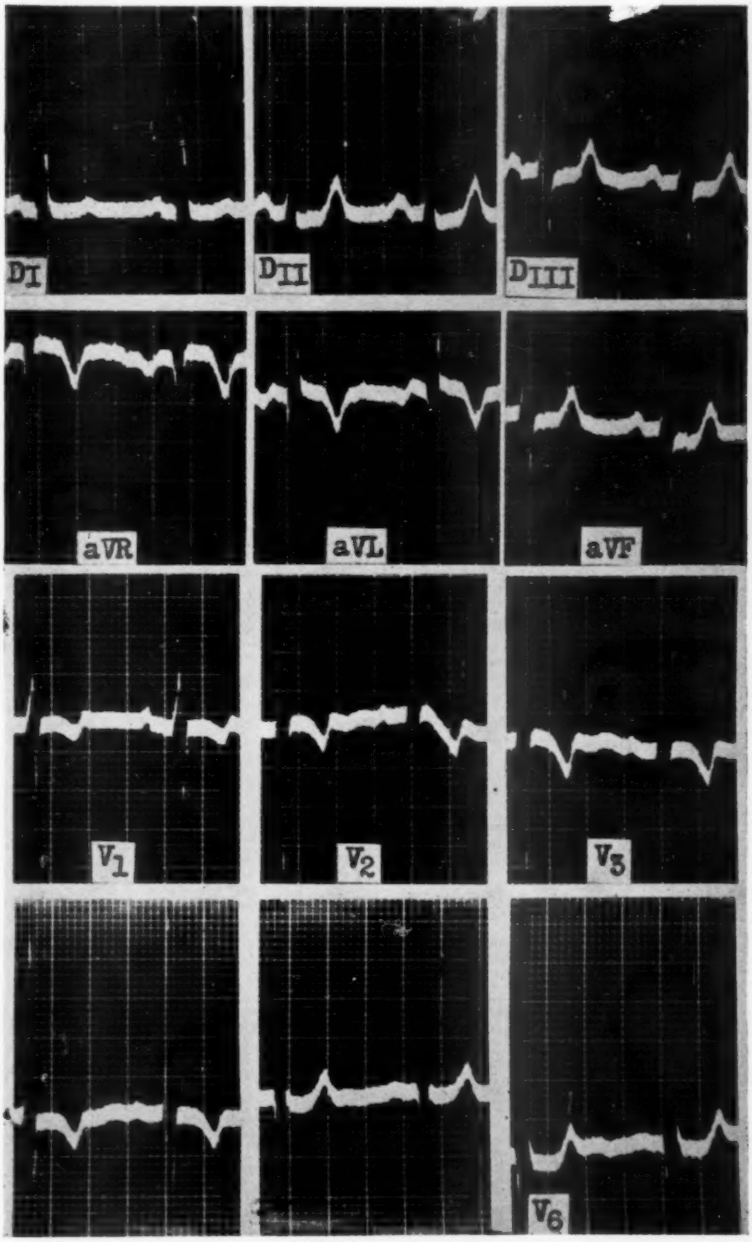
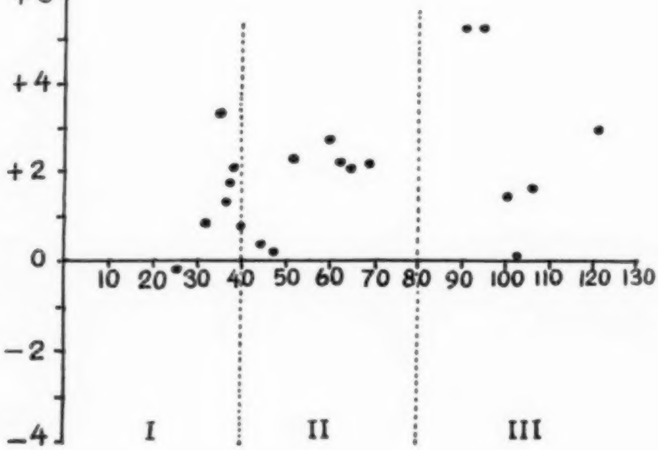
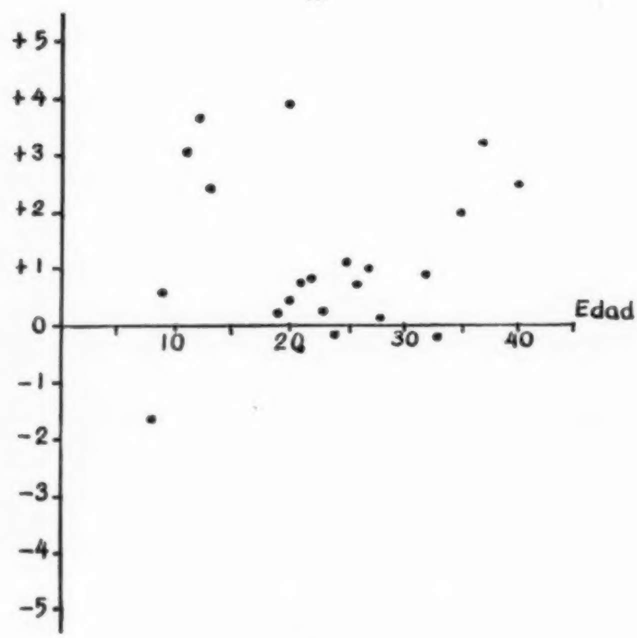


Fig. 11 (J.M.L., 12 yrs. old, Reg. 25077).—Patent ductus arteriosus with pulmonary hypertension. Notice (a) the high R wave in the "left epicardial" leads, going out of the tracing in L_{II}, V_5 and V_6, (b) the slurred and delayed R wave in V_1, (c) the high peaked T wave in L_{II}, L_{III}, aV_F, V_5, V_6.

The lack of opposition between $\hat{A}_{QRS}$ and $\hat{A}_T$ in rheumatic aortic insufficiency had been described by Jinich.[39] We have also found[14] a positive T wave (higher than normal) in the "left ventricular leads" in 84 per cent of twenty-five cases of isolated rheumatic aortic insufficiency (Figs. 12,*B*, and 13). On the contrary, in syphilitic aortic regurgitation, a flat or negative T wave is the rule in such leads, probably due to incomplete left bundle branch block[32] or to coronary insufficiency.



A.



B.

Figure 12.—*A*, Relative voltage of the T wave in twenty-one cases of patent ductus arteriosus as compared to the normal mean value which is made to coincide arbitrarily with zero. Abscissae indicate the systolic right ventricular pressure (mm. Hg).

B, Relative voltage of the T wave in twenty-five cases of rheumatic "pure" aortic regurgitation, not receiving digitalis. The zero line coincides arbitrarily with the normal mean value of the T wave for each particular case. Abscissae indicate the age of the patient. Notice a great preponderance of positive values.

After Brock's operation for Fallot's tetralogy (which increases the pulmonary blood flow, thus producing a diastolic overloading of the left ventricle), Brock and Campbell have reported[7,8] some changes of the T wave, similar to those found in patent ductus arteriosus with pulmonary hypertension (a flat or negative T_1 and a high T_3). These changes, ascribed by Brock and Campbell to the ventriculotomy, are of late appearance and are not preceded or accompanied by an elevated S-T segment; so we feel they are more probably due to the hemodynamic changes brought on by the operation.

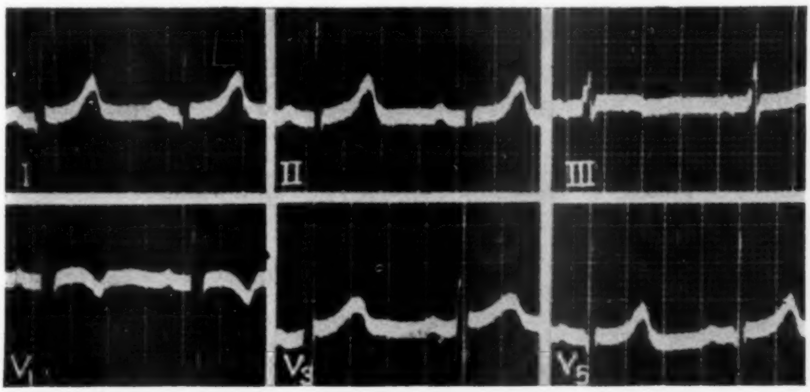


Fig. 13 (S.L.V., 13 yrs. old, Reg. 18671).—Rheumatic "pure" aortic regurgitation. Notice the high peaked T waves in the "left ventricular leads" (L_I, L_{II} and V_5).

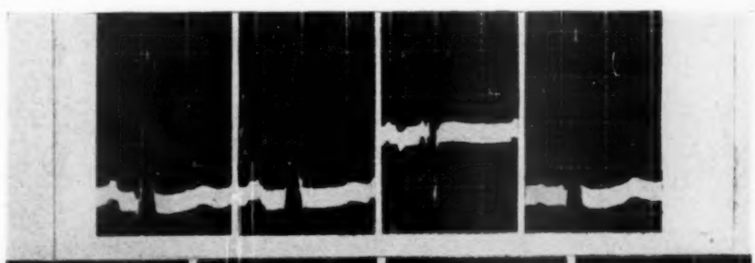


Fig. 14 (C.M.C., 47 yrs. old, Reg. 14179).—Upper row, Standard leads and V_5 before operation; blood pressure 200/130. Lower row, The same leads after Smithwick's sympathectomy; blood pressure 140/90. Notice the "improvement" of the T wave as the pressure drops.

2. *Systolic Overloading of Left Ventricle.*—The most important feature of the electrocardiogram of systolic overloading of the left ventricle is given by a sustained, delayed repolarization of the left ventricle, so producing a negativity of the T waves and/or S-T segment upon the "left ventricular leads," as well as an

opposition between $\hat{A}_{QRS}$ and $\hat{A}_T$.[10,19,39,69]* The flattening or negativity of the T wave, with a depression of the S-T segment in V_5 or V_6, is a well-known fact in arterial hypertension.[28,30,39,43,56,67] It is also widely accepted that a lowering of the mean aortic pressure in hypertensive patients who have been treated by

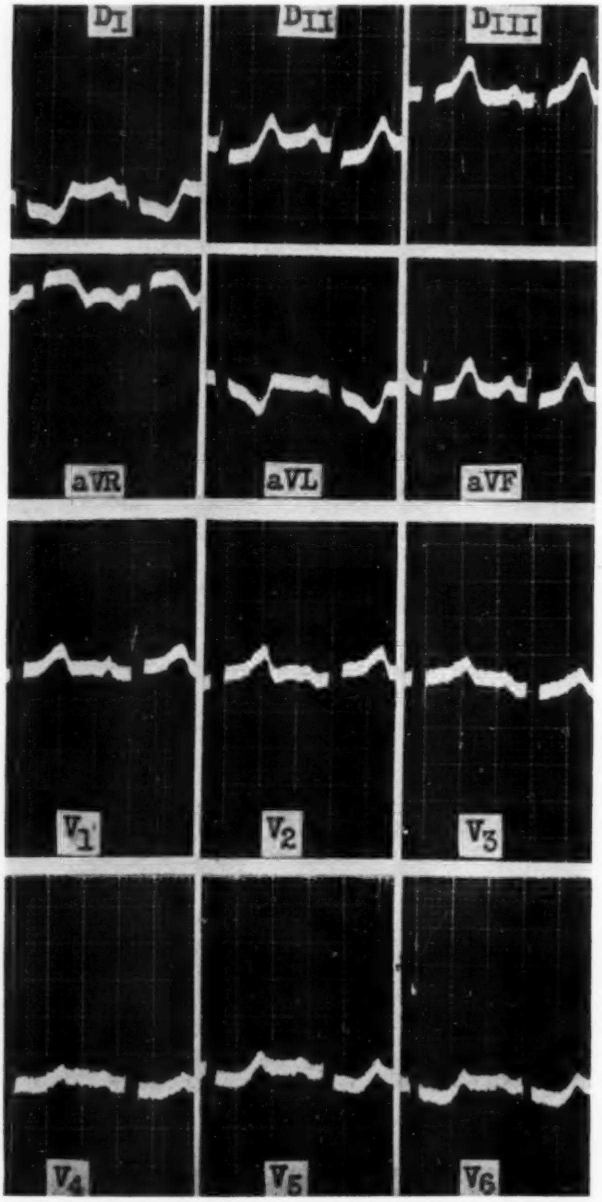


Fig. 15.—Same case as in Fig. 11. Six days after ligation of the ductus arteriosus. Notice the marked S-T segment depression and the flattening of the T waves in the "left epicardial" leads. The patient had not received digitalis after the operation.

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*An incomplete (less frequently a complete) left bundle branch block is often seen in systolic overloading of the left ventricle, but we think it is rather due to a coronary complication, because this is a common finding among patients with hypertension or aortic stenosis and because an incomplete left bundle branch block is also seen commonly in luetic aortic regurgitation, which produces a diastolic overloading not a systolic overloading of the left ventricle.

sympathectomy,[6,63,73] drugs,[31,58] or merely by rest and diet[44,61] is followed by a positivization of the T waves (Fig. 14). The negativity of the T wave is also an early and common finding among the cases of aortic stenosis.[2,4,65]

But it is undoubtedly in the case of a diastolic overloading of the left ventricle which is transformed into a systolic overloading of the same ventricle, where one can demonstrate more easily that a systolic overloading may produce a negativity of the T wave. In this respect we have seen,[11] a few days after the ligation of a patent ductus arteriosus (this operation makes the diastolic overloading of the left ventricle disappear while the systolic loading increases because of a higher aortic pressure), a transitory flattening or even negativity of the T waves appear-

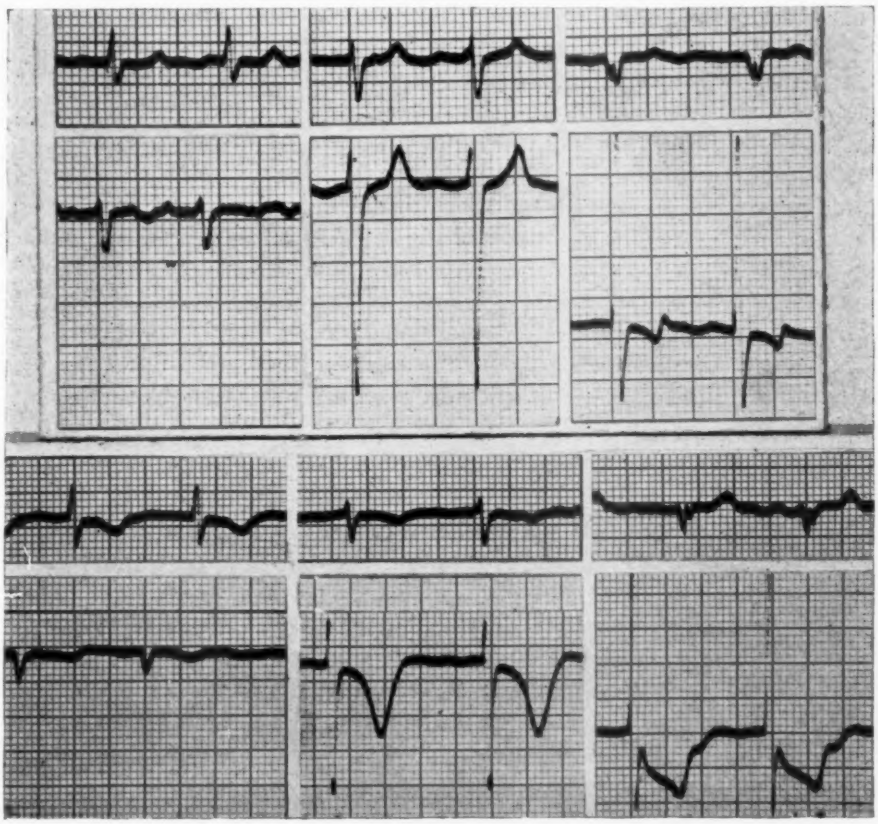

Fig. 16.—Standard leads, V_1, V_3, and V_5, before (upper tracing) and thirty hours after (lower tracing) surgical ligation of a femoral A-V fistula. Same case as Fig. 7. Notice after the operation a marked negativity of the T wave and a negative displacement of the S-T segment in L_I, V_3 and V_5. The electrical axis of the T wave as well as the ventricular gradient became deviated to the right as it happens in lateral myocardial "ischemia."

ing in the "left ventricular leads" which formerly showed a high T wave, despite the decrease of the left ventricular work (Fig. 15). This phenomenon was independent of the heart rate and was never accompanied by substernal pain or worsening of the clinical conditions. We have recently been able to show[15] the same effect after the transitory occlusion of an arteriovenous aneurysm and,

to a greater extent, after its surgical treatment. Thirty hours after the operation, the T waves were deeply negative and the S-T segment was markedly depressed in the "left ventricular leads" (Fig. 16), while the patient showed a notable improvement in the clinical condition as well as in the heart size, without having signs of coronary insufficiency.

DISCUSSION

Although we do not know the ultimate mechanism of production of the electrocardiographic changes in the different types of overloadings, we want to present the possible clues to the electrogenesis of these tracings.

1. The relation between a right bundle branch block and a diastolic overloading of the right ventricle suggests that a dilatation of the cavity is an intermediary factor, as it is always present in any diastolic overloading. Fahr[29] considers that the cause is "an increase in the length of the conduction pathway." Rosenblueth[66] has suggested that if the conduction system follows the laws of conductivity found in nerve fibers (where conductivity is higher as the fiber cross-sectional area increases), dilatation of the cavity could stretch the fibers of the conduction system so decreasing their conductivity. Wilson and associates' explanation of right bundle branch block in cases of acute cor pulmonale[74] as being caused by "a decreased density of the junctions between Purkinje and ordinary muscle in certain areas, as a result of dilatation" is also worthy of consideration. Both explanations are functional rather than anatomic. An anatomic injury of the conduction system seems less likely to occur,[57] because (a) a right bundle branch block easily appears and disappears in acute cor pulmonale, (b) Valsalva's or Müller's test readily modifies an incomplete right bundle branch block, and (c) the electrical signs of right bundle branch block diminishes after the surgical treatment in our case of arteriovenous aneurysm.

2. The high R wave in V_1 in case of systolic overloading of the right ventricle must be related to a more permanent factor, perhaps to hypertrophy of the free wall of the right ventricle. We believe this is the case, as we have observed[16] some cases of patent ductus arteriosus complicated by pulmonary hypertension in which the surgical ligation considerably lowered the pulmonary pressure while the R wave and its initial slurring in V_1 remained almost unmodified. Furthermore, Zuckermann and associates[77] have shown a correlation between the voltage of the R wave in V_1 and the thickness of the free wall of the right ventricle or that of the interventricular septum.

As for the T wave of an "ischemic" type in V_1, it seems more easily reversible and could be related to factors similar to those acting in the production of negative T waves in systolic overloading of the left ventricle. (See below.)

3. We do not have a satisfactory explanation for the high T wave which is found in the "left ventricular leads" in diastolic overloading of the left ventricle. Ashman and Byer,[1] studying the effect of the heart rate upon the electrocardiogram, had already described a correlation between the systolic output and the magnitude of the ventricular gradient (consequently the magnitude of the T wave). Our cases of diastolic overloading of the left ventricle are a corroboration of this fact, as they have an augmented T wave in the "left ventricular leads"

(so a greater ventricular gradient) as well as an increase of the blood volume which the left ventricle ejects in each systole.* However, these correlations (Ashman and Byer's and ours) cannot be considered as the elucidation of a mechanism; they are merely a description of facts.

The high R waves in the "left ventricular leads" as well as the deep S waves in V_2 or V_3 are not only related to the hypertrophy of the left ventricle but also to the abnormal position of the heart within the thorax, since the absence of the S waves in the standard leads (consequently the forward displacement of the apex) is a frequent finding in rheumatic aortic incompetence and in patent ductus arteriosus.[39]

4. Against what had been considered in previous papers,[10,19,39,69] we believe that the T-wave changes found in systolic overloading of the left ventricle are usually of a "primary" rather than of a "secondary" type, because we have observed variations of the ventricular gradient, as well as T-wave changes which are not accompanied by QRS changes. This "primary" negativity of the T wave in the "left ventricular leads" would indicate that the monophasic electrical systole of those fibers affected by the systolic overloading increases its voltage and its duration.†

But even though these T-wave changes are "primary" and frequently adopt the form found in experimental or clinical ischemia, we do not consider them as actually due to a decreased blood supply (neither a relative nor an absolute ischemia) because (a) they are not accompanied by clinical manifestations of myocardial ischemia, (b) they are neither preceded nor accompanied by electrical signs of an injury current (the S-T segment is depressed instead of being elevated in the leads where the T wave becomes negative), (c) they attain their maximal negativity earlier than in proved cases of coronary ischemia, and (d) they can appear in cases where the total coronary blood flow increases while the total work of the left ventricle decreases (ligation of a patent ductus arteriosus or of an arteriovenous aneurysm).

SUMMARY

1. The authors present electrocardiographic evidence of a different behavior of the heart, according to the type of hemodynamic overloading.

2. They show that diastolic overloading of the right ventricle readily gives rise to an incomplete right bundle branch block.

3. Systolic overloadings of the right ventricle produce a high R wave and a negative, symmetrical T wave in the right precordial leads.

4. Diastolic overloadings of the left ventricle produce an elevation of both the R and the T waves in those leads where the left ventricular potentials are transmitted.

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*The diastolic overloading of the left ventricle, which is the consequence of systolic overloading when the ventricle fails, produces an increase of the diastolic filling without increasing the systolic output. This might be related to the less frequent elevation of the T wave in the "left ventricular leads" in cases of rheumatic mitral insufficiency or of left ventricular failure.

†Patterson and associates,[62] working upon the left ventricle, have shown that mechanical systole is actually increased in systolic overloading, but we do not know of any direct evidence showing what happens on the electrical systole.

5. Systolic overloadings of the left ventricle give rise to a flattening or negativity of the T wave (sometimes of an "ischemic" shape), as well as a depression of the S-T segment in those leads where the left ventricular potentials are transmitted.

REFERENCES

1. Ashman, R., and Byer, E.: The Normal Ventricular Gradient. II. Factors Which Affect Its Manifest Area and Its Relationship to the Manifest Area of the QRS Complex, Am. Heart J. **25**:36, 1943.
2. Balestin, G.: Le rétrécissement aortique calcifié, Arch. d. mal. du coeur **42**:539, 1949.
3. Barber, I. M., Magidson, O., and Wood, P.: Atrial Septal Defect, Brit. Heart J. **12**:277, 1950.
4. Berk, L. H., and Dinnersteen, M.: Calcific Aortic Stenosis: Clinic and Electrocardiographic Study, Arch. Int. Med. **61**:781, 1938.
5. Bing, R. J., Heimbecker, R., and Falholt, W.: An Estimation of the Residual Volume of Blood in the Right Ventricle of Normal and Diseased Human Hearts in Vivo, Am. Heart J. **42**:483, 1951.
6. Bridges, W. C., Johnson, A. L., Smithwick, R. H., and White, P. D.: Electrocardiography in Hypertension, J. A. M. A. **131**:1476, 1946.
7. Brock, R. C., and Campbell, M.: Valvulotomy for Pulmonary Valvular Stenosis, Brit. Heart J. **12**:377, 1950.
8. Brock, R. C., and Campbell, M.: Infundibular Resection or Dilatation for Infundibular Stenosis, Brit. Heart J. **12**:403, 1950.
9. Burchell, H. B.: The Electrocardiogram in Congenital Heart Disease, M. Clin. North America **33**:1157-1177, 1949.
10. Cabrera C., E.: Bases électrophysiologiques de l'electrocardiographie; ses applications cliniques, Paris, 1948, Masson & Cie.
11. Cabrera C., E., Borges, S., and Novelo, S.: La persistencia del conducto arterioso, Arch. inst. cardiol. México **20**:426, 1950.
12. Cabrera C., E., and Estandía, A.: Valvulopatías reumáticas, Arch. inst. cardiol. México **19**:398-419, 1949.
13. Cabrera C., E., and Monroy, J. R.: Systolic and Diastolic Loading of the Heart. I. Physiologic and Clinical Data, Am. Heart J. **43**:661, 1952.
14. Cabrera C., E., and Monroy, J. R.: Unpublished data.
15. Cabrera C., E., and Monroy, J. R.: Repercusión de la hemodinámica sobre el electrocardiograma en un caso de fístula arteriovenosa, Arch. inst. cardiol. México **21**:457, 1951.
16. Chávez, I., Limón, R., and Cabrera, E.: Unpublished data.
17. Coelho, E. M., Pinto, R., and Nunes-Lisbon, A.: Pulmonary Stenosis With Large Interatrial Septum Defect and Severe Cyanosis, Cardiología **18**:183, 1951.
18. Cournand, A.: Cardiac Catheterization, New York, 1949, Commonwealth Fund.
19. Cuellar, P. A., Sodi Pallares, D., and Cabrera, E.: Estudio de los vectores $\hat{A}_{QRS}$, $\hat{A}_T$ y $\hat{G}$ en las hipertrofias ventriculares, Arch. inst. cardiol. México **15**:214, 1945.
20. Currens, J.: The Electrocardiogram in Pulmonary Embolism, Proc. Staff Meet., Mayo Clin. **17**:502, 1942.
21. Donzelot, E., Metianu, C., Durand, A., Chiche, A., and Ulad, P.: L'électrocardiograme dans la tétralogie de Fallot (étude de 100 cas), Arch. d. mal. du coeur **44**:97, 1951.
22. Douglas, J. M., Burchell, H. B., Edwards, J. E., and Dry, T. J.: Systemic Right Ventricle in Patent Ductus Arteriosus; Report of a Case With Obstructive Pulmonary Vascular Lesion, Proc. Staff Meet., Mayo Clin. **22**:414, 1947.
23. Dry, T. J.: Atrial Septal Defects, M. Clin. North America **32**:895, 1948.
24. Durant, T. M., Long, J., and Oppenheimer, M.: Pulmonary (Venous) Air Embolism, Am. Heart J. **33**:269, 1947.
25. Durant, T. M., Ginsburg, I. W., and Roesler, H.: Transient Bundle Branch Block and Other Electrocardiographic Changes in Pulmonary Embolism, Am. Heart J. **17**:423, 1939.
26. Edwards, J. E., DuShane, J. W., Alcott, D. L., and Burchell, H. B.: Thoracic Venous Anomalies. III. Atresia of the Common Pulmonary Vein, the Pulmonary Veins Draining Wholly Into the Superior Vena Cava, Arch. Path. **51**:446, 1951.
27. Espino Vela, J., Velazques, T., and Fuenmayor, A.: Anomalía congénita de la arteria coronaria derecha. Presentación de un caso, Arch. inst. cardiol. México **21**:686, 1951.
28. Evans, E., Mathews, M., and White, P. D.: The Electrocardiogram in Hypertension, Am. Heart J. **30**:140, 1945.
29. Fahr, G.: An Analysis of the Spread of the Excitation Wave in the Human Ventricle, Arch. Int. Med. **25**:146, 1920.
30. Fishberg, A.: Hypertension and Nephritis, Philadelphia, 1944, Lea & Febiger.
31. Freis, E. D., and Stanton, J. R.: A Clinical Evaluation of Veratrum Viride in the Treatment of Essential Hypertension, Am. Heart J. **36**:723, 1948.

32. Friedland, Ch., Sodi Pallares, D., Soberón, J., and Fishleder, B.: El electrocardiograma en el diagnóstico diferencial de las insuficiencias aórticas reumática y sifilítica, Arch. inst. cardiol. México **19**:341, 1949.
33. Goldberger, E., and Schwartz, S. P.: Electrocardiograms in Chronic Pulmonary Disease; Theoretical Interpretation, Am. Rev. Tuberc. **53**:34, 1946.
34. Gordon, A., and Goldberg, H.: Correlation of the Electrocardiographic Pattern of Right Ventricular Hypertension in Congenital Heart Disease, AM. HEART J. **42**:226, 1951.
35. Gorlin, R., Haynes, F. W., Goodale, W. T., Sawyer, C. G., Dow, J. W., and Dexter, L.: Studies of the Circulatory Dynamics in Mitral Stenosis. II, AM. HEART J. **41**:30, 1951.
36. Grishman, A., Brahms, S. A., Gordon, A., and King, F. E.: Aberrant Insertion of Pulmonic Veins, J. Mt. Sinai Hosp. **17**:336, 1951.
37. Grishman, A., Poppe, I. M., Simpson, R. S., and Sussman, M. L.: Roentgenographic and Angio-Cardiographic Aspects of Abnormal Insertion of Pulmonary Veins, Am. J. Roentgenol. **62**:500-508, 1949.
38. Herrmann, G. R., and Schofield, N. D.: The Syndrome of Rupture of Aortic Root or Sinus of Valsalva Aneurysm Into the Right Atrium, AM. HEART J. **34**:87, 1947.
39. Jinich, B. H.: Estudio electrocardiográfico de las hipertrofias ventriculares, México, 1947, Edición del inst. cardiol. México.
40. Johnson, J. B., Ferrer, I., West, R., and Cournand, A.: The Relation Between Electrocardiographic Evidence of Right Ventricular Hypertrophy and Pulmonary Arterial Pressure in Patients With Chronic Pulmonary Disease, Circulation **1**:536, 1950.
41. Johnson, R. E., Wermer, P., Kruchner, M., and Cournand, A.: Intermittent Reversal of Flow in a Case of Patent Ductus Arteriosus, Circulation **1**:1293, 1950.
42. Joly, F., Carlotti, J., Sicot, J., and Piton, A.: Cardiopathies congénitales. II. Les trilogies de Fallot, Arch. d. mal. du coeur **43**:687, 1950.
43. Katz, L. N.: Electrocardiography, Philadelphia, 1949, Lea & Febiger.
44. Kempner, W.: Some Effects of the Rice Diet Treatment of Kidney Disease and Hypertension, Bull. New York Acad. Med. **22**:358, 1946.
45. Knutson, J. R. B., Taylor, B. E., Pruitt, R. D., and Dry, T. J.: Anomalous Pulmonary Venous Drainage Diagnosed by Catheterization of the Right Side of the Heart. Report of 3 Cases, Proc. Staff Meet., Mayo Clin. **25**:52, 1950.
46. Kossmann, Ch., Berger, A. R., Brumlik, J., and Briller, S. A.: An Analysis of Causes of Right Axis Deviation Based Partly on Endocardial Potentials of the Hypertrophied Right Ventricle, AM. HEART J. **35**:309, 1948.
47. Krumbhaar, E. B.: Note on Electrocardiographic Changes Accompanying Acutely Increased Pressure Following Pulmonary Artery Ligature, Am. J. M. Sc. **187**:792, 1934.
48. Kuo, P. T., and Vander Veer, J.: Electrocardiographic Changes in Pulmonary Embolism With Special References to an Early and Transient Shift of the Electrical Axis of the Heart, AM. HEART J. **40**:825, 1950.
49. Laham, J., and Gerbaux, A.: Les principaux types électrocardiographiques du "coeur pulmonaire aigu" (étude de 58 cas), Arch. d. mal. du coeur **44**:328, 1951.
50. Lenègre, J., Carouso, G., Spira, R., and Maurice, P.: Les raports de la pression ventriculaire droite moyenne avec le complexe QRST et l'épaisseur de la paroi du ventricule droit, Arch. d. mal. du coeur **42**:477-497, 1949.
51. Lequime, J., and Denolin, H.: La communication interauriculaire. Etude clinique et physiopathologique de 4 cas, Acta cardiol. **5**:302-318, 1950.
52. Littmann, D.: Ventricular Strain and Ventricular Hypertrophy, New England J. Med. **241**:363-367, 1949.
53. Love, W. S., Brugler, G. W., and Winslow, N.: Electrocardiographic Studies in Clinical and Experimental Pulmonary Embolization, Ann. Int. Med. **11**:2109, 1938.
54. Marchal, G., Duhamel, G., and Bousquet, G.: Sur quatre cas de coeur pulmonaire aigu, Arch. d. mal. du coeur **44**:1, 1951.
55. Marquis, R. M.: Unipolar Electrocardiograms in Pulmonary Stenosis, Brit. Heart J. **13**:89, 1951.
56. Master, A. M.: The Electrocardiogram and X-ray Configuration of the Heart, Philadelphia, 1942, Lea & Febiger.
57. Master, A. M., Kalter, H., Dack, S., and Jaffe, H. L.: The Relation Between Bundle Branch Block and Cardiac Enlargement, AM. HEART J. **20**:186, 1940.
58. Meilman, E., and Krayer, O.: Clinical Studies on Veratrum Alkaloids, Circulation **1**:204, 1950.
59. Micks, R. H.: Congenital Aneurysms of All Three Sinuses of Valsalva, Brit. Heart J. **2**:63, 1940.
60. Myers, G. B., Klein, H. A., and Stofer, B. E.: The Electrocardiographic Diagnosis of Right Ventricular Hypertrophy, AM. HEART J. **35**:1, 1948.
61. Palmer, S. R.: "Improvement" in the Hypertensive Pattern of the Electrocardiogram, Ann. Int. Med. **34**:712, 1951.
62. Patterson, S. W., Piper, H., and Starling, E. H.: The Regulation of the Heart Beat, J. Physiol. **48**:465, 1914.

63. Peet, M. M., and Isberg, E. M.: The Surgical Treatment of Arterial Hypertension, J. A. M. A. **130**:467, 1946.
64. Pellon, R., and Sodi Pallares, D.: Significado clínico del retardo en la inscripción de la deflexión intrínseca en precordiales derechas, Arch. inst. cardiol. México **18**:694, 1948.
65. Rodriguez, M. I., and Sodi-Pallares, D.: Estenosis aórtica; estudio electrocardiográfico, Arch. inst. cardiol. México **21**:1, 1951.
66. Rosenblueth, A.: Inst. of Physiology, Mexico. Personal communications.
67. Rykert, H. E., and Hepburn, J.: Electrocardiographic Abnormalities Characteristic of Certain Cases of Arterial Hypertension, Am. Heart J. **10**:942, 1935.
68. Snyder, G. A. C., and Hunter, W. C.: Syphilitic Aneurysm of Left Coronary Artery With Concurrent Aneurysm of a Sinus of Valsalva and an Additional Case of Valsalva Aneurysm Alone, Am. J. Path. **10**:757, 1934.
69. Sodi-Pallares, D.: Nuevas bases de la electrocardiografía, Mexico, 1951, Prensa méd mexicana.
70. Sodi-Pallares, D., Bisteni, A., and Herrmann, G. R.: Some Views of the Significance of the qR and QR Type Complexes in the Right Precordial Leads in the Absence of Myocardial Infarction, Am. Heart J. **43**:716, 1952.
71. Vass, A., and Keller, Mc. J.: Drainage of Pulmonary Veins Into Coronary Sinus, Am. J. Dis. Child. **78**:906, 1949.
72. Vizcaíno, M., Vaquero, M., and Pellon, I. R.: Comunicación interauricular, Arch. inst. cardiol. México. To be published.
73. White, P. D., Smithwick, R. H., Mathews, W., and Evans, E.: The Electrocardiogram in Hypertension. II. The Effect of Radical Lumbodorsal Sympathectomy, Am. Heart J. **30**:165, 1945.
74. Wilson, F. N., Rosenbaum, F., and Johnston, F. D.: Interpretation of the Ventricular Complex of the Electrocardiogram. From Advances in Internal Medicine, Vol. II. New York, 1947, Interscience Publisher, Inc.
75. Zuckermann, R., Cabrera, E., and Estandía, A.: Maniobras de Valsalva y de Müller en el bloqueo incompleto de rama derecha, Arch. inst. cardiol. México **20**:327-337, 1950.
76. Zuckermann, R., Cabrera, E., Fishleder, B. L., and Sodi Pallares, D.: Electrocardiogram in Chronic Cor Pulmonale, Am. Heart J. **35**:421-437, 1948.
77. Zuckermann, R., Cisneros, F., and Novelo, S.: El electrocardiograma en Algunas Cardiopatías Congénitas, Arch. inst. cardiol. México **21**:61, 1951.
78. Zuckermann, R., Estandía, A., Zamora, J., and Barbato, E.: Cor pulmonale agudo, Arch. inst. cardiol. México **18**:582, 1948.
79. Zuckermann, R., Rodríguez, M. I., Sodi Pallares, D., and Bisteni, A.: Electropathology of Acute Cor Pulmonale, Am. Heart J. **40**:805-824, 1950.

DIRECT VENOUS PRESSURE DETERMINATIONS BY USE OF A NEW INSTRUMENT

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IN RECENT years a number of instruments have been introduced for the direct determination of venous pressure. Of these, that[1] used for determination of tissue pressure has certain advantages, including the employment of a small needle which makes it possible to enter and record pressure in small veins. Recently, this instrument has been modified[2] by the replacement of the U-tube water manometer with a bellows system. This change made the instrument more compact and portable. The present report records some experiences with a further modification* whereby an important and novel change in the bellows system not only eliminates the necessity for an additional recorder but also simplifies the readings and manipulations.

THE INSTRUMENT

The essential change in the instrument consists of a drastic reduction in the total dead air space to such a degree that one turn through 360 degrees of a screw compressing the bellows permits a range of pressure from 0 to 600 mm. of water. For this reason a dial securely fastened to the screw compressing the bellows may be calibrated through the 360 degrees in millimeters of water and so marked that immediate direct readings of the pressure may be made upon it.

In essence, the instrument (Fig. 1) consists of a glass adapter approximately 10.0 cm. in length with a bore of 1.0 mm. Transverse scratch marks are made on the adapter at 1.0 mm. levels to aid in the location of movements of a meniscus. A metal frame, or holder, facilitates the attachment to one end of the adapter of a 24- to 27-gauge needle of the type commonly used for subcutaneous injections and, to the other end, of a rubber or plastic tubing which leads through a valve (Fig. 1, *V*) to a bellows system in which the air pressure may be raised or lowered by turning the screw (Fig. 1, *S*) mentioned above, and the pressure in the system determined by reading directly the value on the previously calibrated dial. The valve, *V*, is so arranged that a turn in one direction opens the system to atmospheric pressure and a turn in the opposite direction closes this opening and creates a single air system opening to the atmosphere only through the attached needle.

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*The instrument was designed by Mr. G. Morgavi, Jr.

TECHNIQUE

A sterile glass adapter and needle are prepared. The valve, *V*, is closed, creating a single air system completely closed to the atmosphere down to the needle opening. The adjustment screw, *S*, of the bellows is turned counterclockwise as far as it will go. This increases the air space in the system to a maximum and shows on the dial a pressure reading of zero. The point of the needle is then placed, with sterile precautions, into a solution of sterile normal saline or 2 per cent sodium citrate solution and the screw of the bellows turned until a series of bubbles, produced by air being displaced from the closed system through the needle, emerge from the end of the needle. The screw, *S*, is then reversed, still keeping the needle point below the surface of the solution. The negative pressure thus produced by increasing the dead space in the bellows causes the solution to be drawn up into the needle and into the glass adapter. When the meniscus

Fig 1.—Photograph of instrument prepared for use. Size of instrument may be judged from the adapter, which is 10 cm. in length.

is about one-third of the way up the adapter, the valve, *V*, is opened and the needle removed from the solution. Atmospheric pressure is thus introduced above the meniscus and the screw, *S*, may then be turned to read zero (atmospheric) pressure. The valve, *V*, is then again closed. At this point the *exact* location of the meniscus must be noted by sighting it off against the transverse scratches on the adapter, for when the reading is finally made the meniscus must be brought back *to this exact point* or there will be an error in the determination. Then in the usual fashion the skin over the vein is prepared for venipuncture and the site of puncture brought to proper level for the determination. The instru-

ment itself need not be at this level, only the needle penetrating the vein. Upon insertion of the needle into the vein, the meniscus in the adapter will immediately and rather rapidly begin to rise as venous blood enters the needle. The screw, *S*, is then promptly turned clockwise, not only until the meniscus ceases to move but until there is no movement of the meniscus when it is brought to the exact location in the adapter that it occupied just before venipuncture was made. Fine adjustments are made at this precise point *until the meniscus is flat* at right angles to the wall of the adapter rather than having its usual U-shaped surface. At this point the pressure may be read directly from the dial and taken as the venous pressure. Since the meniscus is not in motion when the determination is made, the small bore of the needle does not interfere with the determination. The needle may then be removed from the vein. Because of the positive pressure in the closed system, the fluid, partially blood tinged, will escape from the end of the needle. The screw may be turned farther to facilitate emptying of the adapter and needle, both of which are then detached and resterilized for future use. By keeping on hand a number of such sterile needles and adapters, along with sterile saline or citrate solution, the physician may take repeated venous pressures on different subjects without the necessity for a sterilizer at the time. The absence of a water manometer makes the instrument easily portable and it may be stored, together with the sterile equipment, in a small space in a physician's bag for use outside the hospital or office.

Two final words about technique are necessary. First, the capillarity in the glass adapter is slightly under 2 cm. of water. This error is corrected by holding the level of the meniscus about 2 cm. above the vein during the determination. Second, the fluid in the adapter should never be permitted to go above the adapter into the tubing. If this occurs, the tubing must be heat-sterilized to prevent the possible transmission of serum hepatitis and other infections. After several manipulations, one becomes adept at increasing the pressure in the system as the vein is entered so that the meniscus does not go above the upper one-third of the adapter.

RESULTS

The author has tested the apparatus against varying levels of water in an upright glass tube turned at right angles near its lower end and capped at the lower opening with a rubber diaphragm. By inserting the needle into the rubber diaphragm, the pressure may be taken just as the venous pressure is determined. In repeated tests over several months at pressure levels from 30 to 300 mm. of water, errors of 2 to 5 mm. of water were observed, and included the errors of the entire procedure, those of the instrument, readings of the meniscus, and all personal factors.

In ten patients with various venous pressures, the technique has been compared with direct determinations made with a saline manometer and syringe. Results are shown in Table I. It may be seen that agreement was satisfactory and that differences to 16 mm. of water occurred. These errors, of course, represent those of both techniques as well as some possible slight variation in the relationship of the veins-to-heart level between determinations.

TABLE I. ESTIMATION OF VENOUS PRESSURE IN SAME PATIENTS AT SAME TIME BY PRESENT METHOD AND BY SALINE MANOMETER

SUBJECT	DIAGNOSIS	VENOUS PRESSURE (mm. H_2O) ANTECUBITAL VEIN, HEART LEVEL		DIFFERENCE BETWEEN DETERMINATIONS
		PRESENT METHOD	SALINE MANOMETER	
H. J.	Normal	92	101	9
B. W.	Normal	78	74	4
J. K.	Normal	86	85	1
M. S.	Constrictive pericarditis	274	290	16
B. M.	Decompensated arteriosclerotic heart disease	172	168	4
W. T.	Decompensated arteriosclerotic heart disease	140	148	8
J. D.	Decompensated arteriosclerotic heart disease	160	160	0
J. M.	Decompensated rheumatic heart disease	134	140	6
B. H.	Aortic aneurysm	176	170	6
R. H.	Decompensated hypertensive heart disease	198	192	6

DISCUSSION

The notable advantages of the instrument are the facility with which it may be used on small veins, the immediately apparent readings, and the simplicity of storing, transporting, and reusing the apparatus. There are certain minor disadvantages observed by the operator when he first uses it. These are easily overcome by a few trials of the instrument. The small dead air space, which is the heart of the instrument in that it permits complete readings on the partial single turn of a dial, makes it necessary that (1) the meniscus be brought back exactly to the starting position and "flattened out," and (2) a deft maneuver, to stop the rise of the meniscus above the upper third of the adapter, be carried out to prevent possible contamination of the plastic tubing. However, after a few trials, the operator should have no difficulty.

Obviously, too, the instrument may be adapted for measurement of other pressures (tissue, spinal fluid).

SUMMARY

The use of an apparatus for direct determination of venous pressure is described. Its advantages include:

1. The facility with which it may be used on small veins.
2. The ease with which it may be stored and transported.
3. The ease with which results are read.
4. Opportunity for frequent reuse in the absence of a sterilizer.

Comparison of this technique with a standard technique for direct determination of venous pressure showed satisfactory results.

REFERENCES

1. Burch, G. E., and Sodeman, W. A.: A Direct Method for the Determination of Venous Pressure; Relationship of Tissue Pressure to Venous Pressure, J. Clin. Investigation **18**:31, 1939.
2. Burch, G. E., and Winsor, T.: The Phlebomanometer: A New Apparatus for Direct Measurement of Venous Pressure in Large and Small Veins, J. A. M. A. **123**:91, 1943.

APICAL DIASTOLIC MURMURS IN CONGENITAL HEART DISEASE

The Rarity of Lutembacher's Syndrome

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THE MITRAL diastolic murmur was classically described by Duroziez[1] in 1862. White[2] refers to it as a rumbling, usually low-pitched, rarely blowing murmur, best heard at the apex. It may be exaggerated when the patient lies on his left side and when the cardiac output increases (that is, after exercise). It is separated from the second heart sound by an appreciable interval. The murmur is best detected by the open-bell stethoscope held lightly against the chest wall.

Such a murmur is commonly accepted by practitioners and cardiologists as conclusive evidence of organic mitral stenosis.[3,4] There is, however, increasing evidence that a host of acquired conditions other than mitral stenosis may cause turbulence giving rise to mitral diastolic murmurs. Among these conditions are gross aortic insufficiency (Austin Flint murmur),[5] myocardial damage,[6] anemia,[7] and hypertension.[8]

Within recent years it has been recognized that a number of congenital heart diseases, that is, patent ductus arteriosus, ventricular septal defect, coarctation of the aorta, may also give rise to apical mitral diastolic murmurs. Paradoxically enough, in cases of another congenital heart disease, atrial septal defect, the presence of an apical diastolic murmur is still commonly regarded as conclusive evidence of coexisting mitral stenosis, that is, Lutembacher's syndrome.

Lutembacher's syndrome "is an auricular septal defect combined with a congenital or acquired mitral stenosis and enormous dilatation of the pulmonary artery," quoting Taussig.[9] The first observation is credited to Louis (1862),[10] but a case was described by Corvisart[11] in 1814. Lutembacher,[12] in 1916, focused attention on this combination as a clinical entity. Numerous papers have been published on the subject since 1916; the most important ones are those of Roesler,[13] McGinn and White,[14] Taussig and associates,[15] Bedford, Papp, and Parkinson,[16] Uhley,[17] and Burrett and White.[18] In addition to these comprehensive reviews, a number of individual case reports are available.

The combination of atrial septal defect with mitral stenosis has been so powerfully impressed on cardiologists that we believe the diagnosis of Lutembacher's

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syndrome is often made solely on the basis of an apical diastolic murmur in a patient with congenital heart disease. Indeed, Taussig says "When a systolic murmur at the base, suggestive of congenital malformation of the heart, occurs in conjunction with a murmur at the apex which is characteristic of a rheumatic infection, the possibility of this malformation (i.e. Lutembacher's syndrome) should always be considered."[9]

The purpose of this paper is to investigate the frequency of apical diastolic murmurs in congenital heart disease, the particular congenital lesions with which they are most commonly associated, and finally to elucidate certain features of Lutembacher's syndrome both from the clinical and pathologic viewpoints.

RESULTS

1. *How Common Are Apical Diastolic Murmurs in Patients With Congenital Heart Disease?*

One hundred consecutive cases of noncyanotic congenital heart disease attending the Cardiac Clinic of the Children's Hospital were studied. All patients with obvious arterial unsaturation were excluded since the purpose of this study was to investigate Lutembacher's syndrome, a lesion not accompanied by cyanosis.

Careful clinical histories were obtained with special reference to rheumatic fever. The physical findings were checked by several observers at our Congenital Heart Clinic and by at least one of the authors. In addition to the routine laboratory procedures, all the patients were subjected to x-ray, fluoroscopic, and electrocardiographic studies. The x-ray findings represent the opinions of the Radiological Department of the Children's Medical Center. The electrocardiograms were taken by one technician on a Sanborn Viso-Cardiette and included the standard limb leads, augmented unipolar limb leads, and unipolar chest leads V_{1-6} with additional leads to the right and left as required. All the cardiograms were analyzed by at least one of the authors. Phonocardiograms were available in about one-third of the patients with mitral diastolic murmurs in this group. The phonocardiographic tracings were taken with a Sanborn twin-beam Stetho-Cardiette following the technique of Rappaport and Sprague.[19] For reference tracings, electrocardiogram Lead II and apex cardiogram were used.

The clinical diagnoses in this group were based on the findings enumerated above and represent, in the majority of instances, the combined opinions of the cardiologists and roentgenologists.

Nineteen patients out of our 100 cases of noncyanotic congenital heart disease studied showed unequivocal apical diastolic murmurs. A summary of our findings in these nineteen patients is found in Table I.

The ages of our patients varied from 10 months to 14 years. There were eleven girls and eight boys in the group. Four patients had past histories suggestive of rheumatic fever; in none of them was this story unequivocal.

All patients had both systolic and diastolic murmurs over their hearts. The systolic murmurs varied in intensity, location, and character according to the particular lesion involved. The diastolic murmurs were all Grade II-III

in intensity, almost always occupying the first rapid-filling period (mid-diastole) and only infrequently the second rapid-filling period (presystole).

The x-ray evidence revealed considerable cardiomegaly in all but one case (No. 7); the electrocardiographic and x-ray evidence pointed to right, left, or combined ventricular hypertrophy, depending on the anatomic lesion.

The final clinical diagnosis was atrial septal defect in six cases, ventricular septal defect in five cases, and truncus arteriosus, as demonstrated by cardiac catheterization, in one patient. In the remaining seven patients, no single definite diagnosis was determined.

In conclusion, then, we can say that an apical diastolic murmur is rather common in congenital heart disease; we found it to be present in 19 per cent of our 100 patients. All the patients showed some degree of cardiac enlargement. The enlargement involving the right side and the left side occurred with about equal frequency. An anatomic diagnosis was made with relative certainty in eleven of the nineteen patients.

2. *Which Are the Congenital Heart Lesions Most Frequently Accompanied by Apical Diastolic Murmurs?*

A second series of twenty patients with congenital heart disease and apical diastolic murmurs was selected for intensive study in order to answer this question. The exact nature of the cardiac abnormality in this group was determined not only by the methods referred to in Section 1 but also by cardiac catheterization, thoracotomy, or autopsy. All the patients in this group had phonocardiograms taken by the method cited in Section 1. Our results are summarized in Table II.

There were twelve girls and eight boys in this group, and their ages ranged from 4 to 19 years. Three of our cases showed definite evidence of rheumatic fever in their past histories; and in two additional patients, there was only a suggestion of such possibility. All patients in this group had both systolic and diastolic murmurs over their hearts. The systolic murmurs were all at least Grade IV in intensity and varied as to location and character according to the anatomic lesion. The diastolic murmurs were chiefly in mid-diastole and only infrequently (three instances) in presystole. In three of our four patients with patent ductus arteriosus, the characteristic continuous machinery murmur was present at the second left intercostal space. Graphic registration of these auscultatory phenomena is illustrated in the adjoining phonocardiograms.

Fig. 1,*A*, shows the phonocardiogram in Case No. 2. There is an intense systolic murmur due to the ventricular septal defect. This was described as Grade VI by auscultation and was loudest over the third to fourth left intercostal space parasternally. A mid-diastolic murmur of lower frequency is seen in the phonocardiogram over the apex. This diastolic murmur occurs immediately following the third heart sound and occupies the entire duration of mid-diastole without extending into presystole. The third sound is clearly registered and coincides with the tip of the rapid-filling wave in the apex cardiogram. It is of interest that fourteen months previously this diastolic murmur was not detected, either by auscultation or by phonocardiography. Between these two dates, the only

TABLE I

NAME AND NUMBER	AGE AND SEX	HISTORY OF RHEUMATIC FEVER*	MURMUR DISCOVERED	MURMURS		X-RAY‡		ELECTRO-CARDIOGRAM§	CLINICAL DIAGNOSIS ‖
				SYSTOLIC†	DIASTOLIC	LEFT VENTRICULAR	RIGHT VENTRICULAR		
1. D. S. 363179	4½ yrs. F	—	6 mos.	LSB Grade 4	1. Apical blow 2. LSB early blow	±	++	RVH	VSD
2. K. N. 367570	10 mos. M	—	6 wks.	LSB Grade 4	Apical rumble	+	+	RVH	VSD Pulmonary hypertension
3. M. Z. 358182	3 yrs. 3 mos. F	—	7 mos.	Basal and LSB Grade 4	1. Apical rumble 2. LSB early blow	++	++	RVH	ASD ? PDA
4. L. K.	2 yrs. 7 mos. M	—	9 mos.	Apical Grade 4	Apical rumble	+	+	LVH	Septal defect
5. E. O.	3 yrs. 6 mos. F	—	1 yr.	3 LIS Grade 3	Apical rumble	+	+	RVH	ASD ? Single ventricle
6. M. L.	14 yrs. F	±	5 yrs.	1. Apex Grade 3 2. Aortic Grade 3	Apical rumble	++	+	RBBB	ASD ? RHD
7. S. P. 366697	11 mos. F	—	3 wks.	LSB Grade 4	Apical rumble	—	—	RVH	VSD
8. B. S. 342439	2 yrs. 6 mos. F	—	2 mos.	Xiphoid Grade 5	Apical rumble	++	±	LVH	VSD
9. P. C. 352281	3 yrs. 9 mos. F	—	Birth	LSB Grade 4	Apical rumble	—	++	RBBB	ASD ? Eisenmenger
10. M. T. 287195	7 yrs. 2 mos. M	±	6 mos.	Xiphoid Grade 6	Mid-diastole and presystole Apical	+++	+++	LVH	VSD ? PDA
11. R. J. 349199	4 yrs. M	—	2 yrs.	2 LIS Grade 3	Apical rumble	+	++	RVH	ASD
12. C. T. 369513	12 yrs. 10 mos. F	±	9 mos.	2 LIS Grade 3	Apical rumble	± Calcified mitral valve	++	LVH	ASD MS
13. H. M. 312956	5 yrs. 3 mos. M	—	2 wks.	LSB Grade 4	Apical rumble	+++	+++	LVH	VSD

14. R. B. 365683	2 yrs. 7 mos. F	—	11 mos.	3 LIS Grade 3	Apical rumble	±	++	RVH	ASD
15. C. G. 371764	8 mos. M	—	Birth	3 LIS Grade 3	Apical rumble	±	—	RBBB	??
16. S. S. 350886	3 yrs. M	—	Birth	LSB Grade 5	Apical rumble	+	±	LVH	VSD
17. R. L. 365903	13½ yrs. M	±	1 yr.	2 LIS Grade 5	1. 2 LIS machinery 2. Apical presystole	++	+++	CVH	Truncus arteriosus by catheter
18. S. S. 332128	3 yrs. 5 mos. F	—	3 mos.	LSB Grade 4	Apical rumble	+++	++	RVH	VSD
19. K. E. 354817	4 yrs. 2 mos. F	—	2 yrs.	2 LIS Grade 3	Apical rumble	±	++	RVH	ASD

******History of Rheumatic Fever*
+ Positive
— Negative
± Questionable

†*Murmurs*
LSB Lower left sternal border
2 LIS Second left intercostal space
3 LIS Third left intercostal space

‡*X-ray Enlargement*
± Questionable
+ Definite
++ Considerable
+++ Marked

§*Electrocardiogram*
RVH Right ventricular hypertrophy
LVH Left ventricular hypertrophy
CVH Combined ventricular hypertrophy
RBBB Right bundle branch block

||*Diagnosis*
ASD Atrial septal defect
L.S. Lutembacher's Syndrome
VSD Ventricular septal defect
PDA Patent ductus arteriosus
MS Mitral stenosis
RHD Rheumatic heart disease

TABLE II

NAME AND NUMBER	AGE AND SEX	HISTORY OF RHEUMATIC FEVER*	MURMUR DISCOVERED	MURMURS†		X-RAY‡		ELECTROCARDIOGRAM§	DIAGNOSIS ‖	
				SYSTOLIC	DIASTOLIC	LEFT VENTRICULAR	RIGHT VENTRICULAR		CLINICAL	FINAL
1. C. K. 357761	19 yrs. F	+	8 yrs.	2 LIS Grade 3	Apical rumble	±	++	RVH	L.S.	ASD**
2. L. D. 340294	9 yrs. F	—	Birth	LSB Grade 5	Apical rumble	+	—	LVH	VSD PDA	VSD¶
3. S. P.	4 yrs. F	—	3 yrs.	LSB Grade 4	Apical rumble	+++	+++	CVH	L.S. VSD	VSD**
4. S. L. 250222	8 yrs. F	—	5 mos.	LSB Grade 5	1. 2 LIS blow 2. Apical rumble	—	+++	RVH	ASD L. S. Eisenmenger	ASD¶
5. L. G. 285978	8 yrs. M	—	2 yrs.	3 LIS Grade 5	Apical rumble	+	+	RVH ? LVH	ASD Eisenmenger	Eisenmenger ¶
6. J. M. 362107	13 yrs. F	—	4 mos.	1. LSB Grade 4 Rough 2. Apex Grade 4 Whistle	1. LSB blow 2. Apical rumble	++	++	CVH	Eisenmenger	VSD¶ No pulmonary hypertension
7. R. C. 298564	5 yrs. M	—	7 mos.	LSB Grade 5	Apical rumble	++	—	LVH	VSD	VSD¶
8. W. K. 313098	4 yrs. M	—	6 wks.	LSB Grade 5	Apical rumble	++	++	RVH	VSD	VSD¶ Pulmonary hypertension
9. F. K. 282939	8 yrs. F	—	1 yr. 2 mos.	Basal Grade 3	Apical rumble	++	±	LVH RBBB	Septal defect ? L.S.	PDA***

10.	G. P. 285072	7½ yrs. F	—	1 yr.	2 LIS Grade 4	Apical presystolic	++	++	RVH	L.S.	ASD¶
11.	G. S. 290916	10 yrs. M	—	6 yrs.	2 LIS Grade 4	Apical mid-diastolic and presystolic	++	—	LVH	Coarctation of the aorta with PDA	Same¶
12.	P. G. 300528	8 yrs. F	+	1 yr.	1. 2 LIS Grade 3 2. Apical Grade 3	1. 2 LIS blow 2. Apical rumble	—	++	RVH	L.S. ? PDA	ASD¶
13.	J. H. 337028	11 yrs. M	—	4 yrs.	2 LIS Grade 3	Apical rumble	++	++	RVH	ASD	ASD¶
14.	R. J. 351874	6½ yrs. M	±	2 yrs.	LSB Grade 5	Apical rumble	—	++	RVH	ASD L.S.	VSD¶
15.	L. R. 368155	12 yrs. 8 mos. F	—	1 yr.	2 LIS machinery murmur		++	—	LVH	Coarctation of aorta with PDA	Same***
					Apical Grade 3	Apical rumble					
16.	B. C. HGS 8504	16 yrs. F	+	7 yrs.	Apical Grade 4	Apical rumble	—	++	RVH	MS L.S.	ASD**
17.	G. C. HGS 8384	11 yrs. F	—	6 yrs.	2 LIS Grade 3	Apical rumble	++	++	RVH	ASD L.S.	ASD¶
18.	J. R. 340427	5 yrs. M	—	10 mos.	2 LIS machinery murmur		++	+	CVH	PDA	PDA***
					Apical Grade 3	Apical rumble					
19.	G. R. 342111	9 yrs. F	+	6 yrs.	2 LIS Grade 3	LSB blow	±	++	RVH	L.S.	ASD¶
20.	C. S. 299152	9 yrs. F	—	Birth	LSB Grade 4	Apical rumble	++	+	RVH	ASD L.S.	Single ventricle¶

**History of Rheumatic Fever*

+ Positive
— Negative
± Questionable

†*Murmurs*

LSB Lower left sternal border
2 LIS Second left intercostal space
3 LIS Third left intercostal space

‡*X-ray Enlargement*

± Questionable
+ Definite
++ Considerable
+++ Marked

§*Electrocardiogram*

RVH Right ventricular hypertrophy
LVH Left ventricular hypertrophy
CVH Combined ventricular hypertrophy
RBBB Right bundle branch block

||*Diagnosis*

ASD Atrial septal defect
L.S. Lutembacher's Syndrome
VSD Ventricular septal defect
PDA Patent ductus arteriosus
MS Mitral stenosis

¶Catheter
**Autopsy
***Operation

change in clinical status was a further increase in left ventricular enlargement by x-ray and hypertrophy by electrocardiogram.

Fig. 1,*B*, is the phonocardiogram over the apex in another case of ventricular septal defect (Case No. 3). The systolic murmur is similar to that of the preceding case. However, the diastolic murmur starts somewhat later in diastole, extends into presystole, and shows a considerable admixture of high-frequency vibrations.

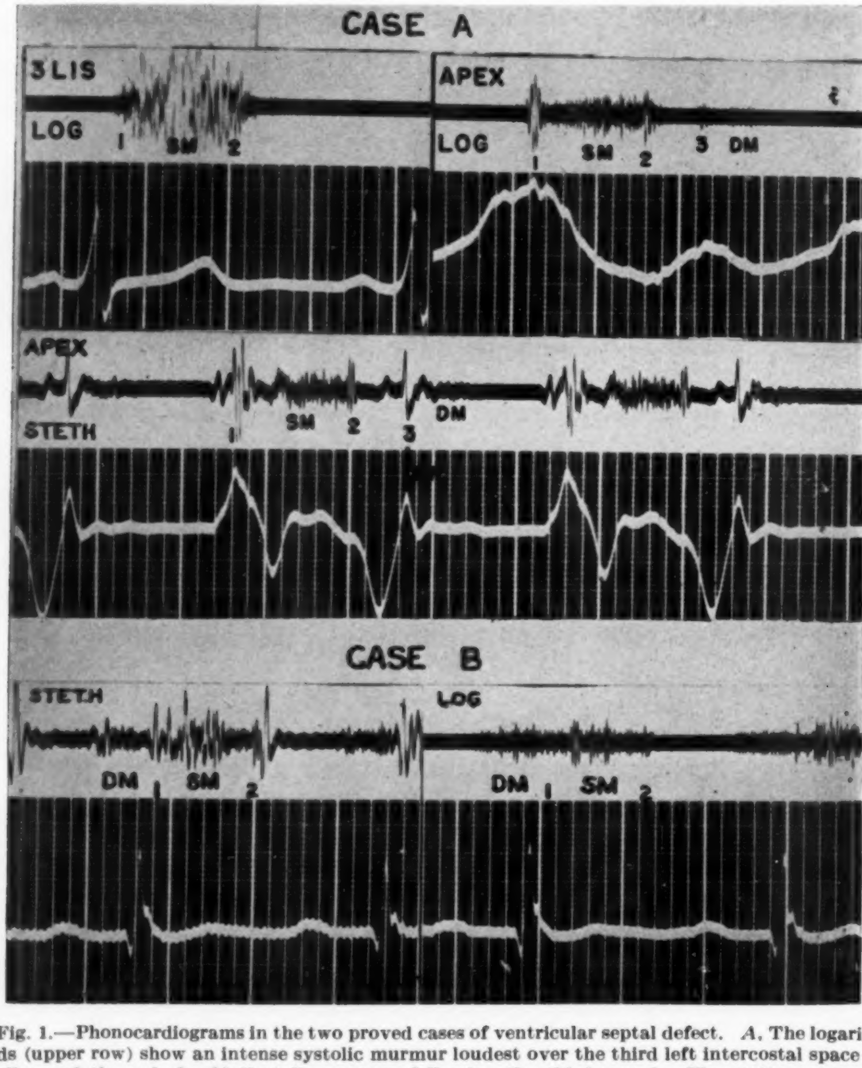

Fig. 1.—Phonocardiograms in the two proved cases of ventricular septal defect. *A*, The logarithmic records (upper row) show an intense systolic murmur loudest over the third left intercostal space parasternally, and the apical mid-diastolic murmur following the third sound. The stethoscopic record (lower tracing) shows the third sound well registered and coincides with the rapid-filling wave (*rf*) of the apex cardiogram. *B*, Stethoscopic and logarithmic phonocardiograms over the apex with the same systolic murmur as in *A* but with the diastolic murmur starting later in diastole and extending into presystole.

Fig. 2 illustrates the findings in Case No. 18 which were characteristic of our patent ductus arteriosus cases. The continuous "machinery-type" murmur

is best registered at the second left interspace. It assumes a crescendo configuration in the late part of systole, culminating in the second sound, and assuming a decrescendo character immediately following it. This murmur is likewise recorded over the apex but its diastolic component is much shorter in this area and fades out soon after the second sound. Another murmur appears at the apex in diastole. This diastolic bruit is of lower frequency than the preceding continuous murmur and starts with the third heart sound, soon diminishes in intensity, and leaves the second rapid-filling period (presystole) silent. The continuous murmur as well as the apical mitral diastolic murmur disappeared postoperatively in all our patients with patent ductus arteriosus.

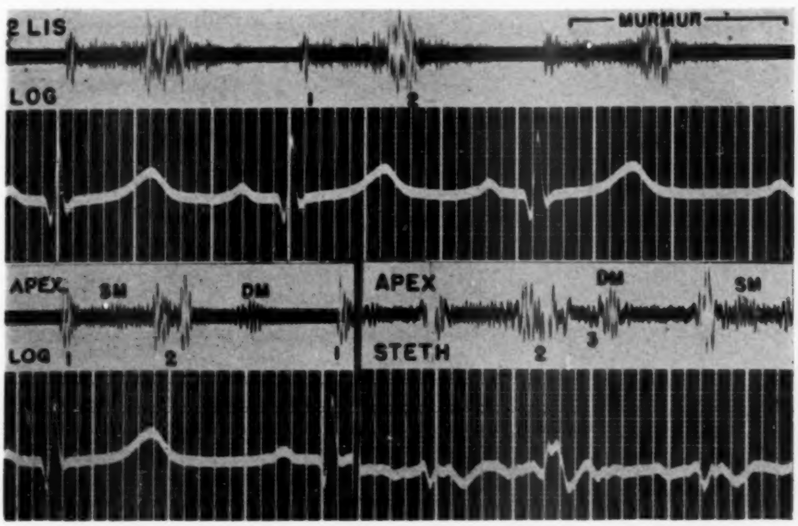

Fig. 2.—Phonocardiograms in a case of patent ductus arteriosus, showing the typical continuous murmur over the pulmonic area. At the apex, this murmur is essentially systolic, but there is now a different murmur in mid-diastole following the third heart sound.

Fig. 3 shows the characteristic phonocardiogram in a patient with atrial septal defect. The upper tracing reflects the auscultatory phenomena at the apex. There is a presystolic murmur without crescendo configuration present, a normal first sound, a systolic murmur, and a split-second sound. The lower tracing pictures the intense systolic murmur at the second left intercostal space with the widely split second sound.

The x-ray and electrocardiographic findings in all our cases revealed cardiac enlargement involving the right and/or the left ventricle.

As may be seen from Table II, the clinical diagnoses were confirmed in the majority of the instances by the subsequent intensive study of these twenty selected cases. The one consistent mistake in our clinical opinion was the frequent consideration of Lutembacher's syndrome in the differential diagnosis. In ten of our twenty patients the combination of atrial septal defect with mitral stenosis was considered seriously enough to appear as the possible diagnosis in the final clinical appraisal of the patient; in the other ten patients, it was unofficially considered from time to time by one or another observer.

The final anatomic diagnoses summarized in Table II revealed eight instances of atrial septal defect, five of ventricular septal defect, four with patent ductus arteriosus, two with Eisenmenger's syndrome, and one case of single ventricle.

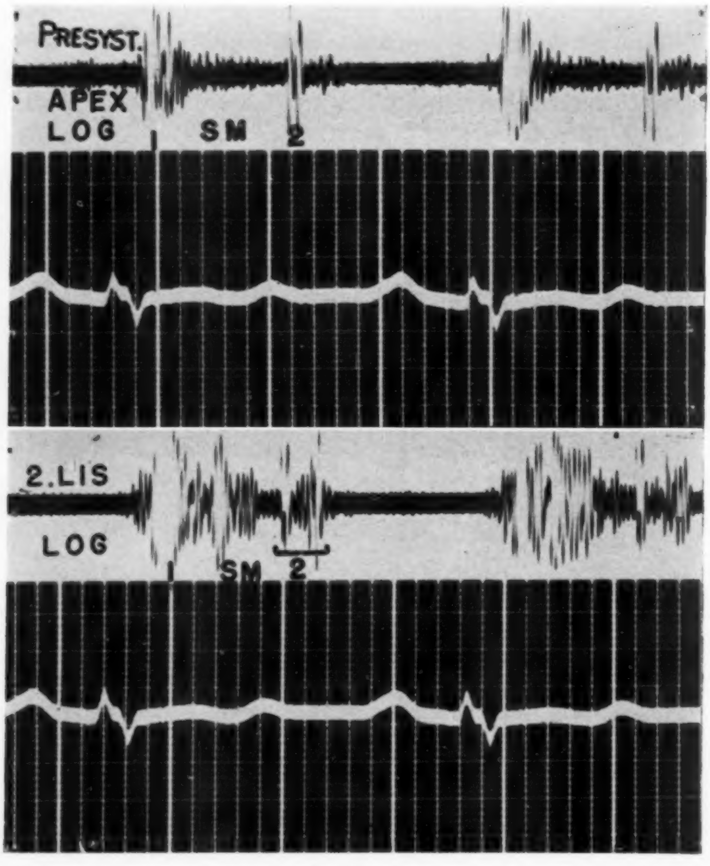

Fig. 3.—Phonocardiogram in a case with atrial septal defect. The upper tracing shows the presystolic murmur without crescendo configuration, the loud first sound, and the decrescendo systolic murmur. At the second left intercostal space, there is seen the intense systolic murmur and the widely split second sound.

In contrast to the clinical expectation, there was not a single case of Lutembacher's syndrome among these twenty intensively studied patients with congenital heart disease and apical diastolic murmurs. Twelve out of our twenty patients could not have had Lutembacher's disease because an atrial septal defect could not be demonstrated in them. The remaining eight patients did have atrial septal defects but an adequate mitral orifice was demonstrated in them either by autopsy (Nos. 1 and 16) or by cardiac catheterization. In four out of six cases of atrial septal defect which were catheterized, we were able to demonstrate the identity of left atrial mean and left ventricular diastolic pressure (Nos. 4, 12, 17 and 19) thus proving the presence of an adequate mitral orifice. In two of our cases (Nos. 10 and 13) with atrial septal defect, the left ventricle was not entered, but the absence of mitral stenosis in these was strongly suggested by normal right atrial, left atrial, and "pulmonary capillary" pressures.

In conclusion, then, it is apparent that a number of different congenital heart diseases may give rise to a mitral diastolic murmur—atrial septal defect, ventricular septal defect, and patent ductus arteriosus being the most common lesions associated with it. Contrary to current clinical belief, we failed to find a single instance of Lutembacher's syndrome among these patients.

3. *How Commonly Is Lutembacher's Syndrome Found in a Large Series of Autopsies?*

Table III summarizes our findings in 25,000 consecutive autopsies in five large Boston hospitals. It may be seen from the table that only five instances of Lutembacher's syndrome were found in this large group. These five cases represent approximately 6 per cent of all the atrial septal defects found among these cases.

TABLE III

HOSPITAL	NO. OF AUTOPSIES	ATRIAL SEPTAL DEFECT	LUTEMBACHER'S SYNDROME
Beth Israēl Hospital	1,915	7	1
Peter Bent Brigham Hospital	5,910	2	—
Deaconess	4,446	3	1
Children's Hospital	5,289	60	2
Massachusetts General Hospital	7,400	15	1
Total	24,960	87	5

It is only fair to point out, however, that this percentage may not be correct since about two-thirds of the cases of atrial septal defect came from the records of the Department of Pathology of the Children's Medical Center and include a rather large number of infants who naturally did not have an opportunity to develop rheumatic mitral stenosis. If we exclude the patients from the Children's Hospital, the percentage of atrial septal defects with Lutembacher's syndrome is approximately 10 per cent.

DISCUSSION

In our experience at the Cardiac Clinic of the Children's Hospital, 19 per cent of the patients with noncyanotic congenital heart disease were found to have apical diastolic murmurs. No figures comparable to this are available from other sources.

Jones, Dolly, and Bullock[20] in 1940 drew attention to mitral diastolic murmurs in uncomplicated cases of patent ductus arteriosus. This observation was later confirmed by Eppinger, Burwell, and Gross[21] in 1941 and by Levine and Geremia[22] in 1947. Ravin and Darley[23] found apical diastolic rumbles in nine of their twenty-one patients with patent ductus arteriosus. All these authors emphasize the fact that following surgical closure or division of the ductus arteriosus the apical murmur disappears. Our own experience, based on the material presented in this paper and on the much larger group of patients seen and followed constantly at the Children's Hospital and the Sharon Cardiovascular Unit

of the Children's Medical Center, is in complete agreement with the findings cited above.

That a ventricular defect, a lesion physiologically very similar to patent ductus arteriosus, may also give rise to an apical diastolic murmur has only recently been emphasized by Wood and his associates,[24] who consider it a frequent phenomenon occurring in at least one-half of the instances of ventricular septal defect and in all cases with large defects. Our experience supports their observations. Five of our twenty intensively studied patients with mitral diastolic murmurs had ventricular septal defects proved with certainty.

The common denominators in patent ductus arteriosus and ventricular septal defect that may explain the origin of this "functional mitral murmur" are increased flow through the mitral valve and left ventricular enlargement. It seems quite reasonable to assume that a mitral valve constructed to accommodate only a certain physiologic flow becomes relatively stenotic when confronted with a flow several times larger than the expected one. That turbulence caused by such a "functionally stenotic" valve may be accentuated by the valve opening into an enlarged left ventricular cavity also seems quite likely. White[25] has recently emphasized the role of an enlarged left ventricle in the creation of mitral murmurs.

The fact that the findings in cases of single ventricle may include an apical diastolic murmur is mentioned by Taussig.[9] One of our patients with single ventricle supports this observation. The theory of the "relative stenosis" of the atrioventricular orifice proposed in connection with patent ductus arteriosus may, we believe, explain the mitral diastolic murmur observed in cases of single ventricle. We believe this theory should also hold in explaining the diastolic murmurs heard at the apex in our two cases with Eisenmenger's syndrome, a lesion hitherto not mentioned as associated with an apical diastolic murmur.

In our experience the most frequent association of apical diastolic murmurs with congenital heart disease occurs in atrial septal defects. The literature supports this thesis to a certain extent. Barber, Magidson, and Wood[26] observed mitral diastolic murmurs in nine of sixty-two cases of atrial septal defect studied by clinical methods.

It is interesting to contrast the acceptance of an apical diastolic murmur as of functional origin in ventricular septal defect or in patent ductus arteriosus with the postulation of its organic nature (signifying true mitral stenosis) in atrial septal defect. Wood[24] states in part: "All mitral murmurs in atrial septal defects were attributed to mitral valve disease, presumably rheumatic." Essentially similar views were expressed by Keith and Forsyth,[27] Cosby and Griffith,[28] and Courter, Felson, and McGuire.[29]

Contrary to this general acceptance of mitral murmurs as being of organic origin in cases of atrial septal defect, we failed to find one case of Lutembacher's syndrome in our cases of atrial septal defect with a mitral diastolic murmur. Neither was there any clinical evidence nor past history suggesting rheumatic heart disease in five of our six clinically diagnosed cases of atrial septal defect with mitral diastolic murmur.

In the absence of any anatomic or physiologic evidence indicating the presence of organic mitral stenosis in these patients, we felt that another explanation for the origin of the murmur would have to be sought. It seemed quite possible that the apical diastolic murmur originates at the site of the atrial defect, at the time of maximal shunt through the defect, that is, mid-diastole or presystole. The septal defect acting as a diaphragm-like orifice between the two atria may create circumstances not very different from those encountered in true mitral stenosis between left atrium and left ventricle. This hypothesis has been proposed by Barber, Magidson, and Wood.[26] A second possibility, explaining the presence of diastolic murmurs, is that it may originate from the right side of the heart due to relative tricuspid stenosis. The greatly dilated tricuspid orifice found at autopsy in these patients makes the latter theory less probable than the former.

Assuming, then, that the majority of the apical diastolic murmurs in congenital heart disease do not originate from truly stenotic mitral valves, it seemed to us worth while to analyze the phonocardiogram of these patients in order to differentiate them from tracings encountered in true mitral stenosis. The following differential diagnostic points were encountered: (1) None of our patients with "functional mitral diastolic murmurs" showed an opening snap of the mitral valve. (2) The diastolic murmur as a rule was confined to mid-diastole. It seldom extended into presystole and only very infrequently assumed crescendo character. (3) The accentuation of the first apical sound, a common observation in mitral valve disease, was not a prominent nor a consistent finding in these cases.

Having established the fact that Lutembacher's syndrome is extremely rare from the clinical viewpoint although apical diastolic murmurs in congenital heart disease are rather common, it seemed to us of paramount importance to determine the frequency of the combination of atrial septal defect with mitral stenosis at autopsy examination. The figures of our autopsy series, representing 25,000 consecutive post mortems in five large Boston hospitals, representing all ages and certainly a large amount of cardiac material, prove without a doubt that Lutembacher's syndrome is as rare on the autopsy table as it is in the clinic.

A number of authors, dealing almost exclusively with adults, have presented material in the past which was in agreement with this view. McGinn and White[14] found only two cases of Lutembacher's disease among 6,800 autopsies at the Massachusetts General Hospital. Cosby and Griffith[28] failed to find a single instance of this syndrome among nineteen autopsies of cases with atrial septal defect, while Gelfman and Levine[30] found only two instances of mitral stenosis with atrial septal defect in 24,000 autopsies in five Boston hospitals. The huge autopsy material of the Mayo Clinic contains twenty-six examples of atrial septal defect. There is only one case of Lutembacher's syndrome among them.[31]

In contrast to this, however, there is a large segment of the literature which suggests that Lutembacher's syndrome is a common condition and includes a considerable portion—even a majority—of all atrial septal defects. Brown,[32] in the latest edition of his book on congenital heart disease, states, "a co-existing mitral stenosis should be suspected in every case of atrial septal defect, despite the absence of any clinical indication of its presence." Taussig[9] states, "it is a

rule rather than the exception to find some lesions of the mitral and aortic valves combined with an atrial septal defect."

In reviewing the literature available on Lutembacher's syndrome, one is struck by several fallacies that may have led to the assumption that this is a common condition. The first and most important source of misunderstanding originates from rather loose use of the term "mitral stenosis." As an example, one may quote Roesler[13] who, presenting from the literature sixty-two cases of atrial septal defect published by fifty-six authors during a 100-year period, found only six cases of "buttonhole stenosis." The rest of them ranged from mitral insufficiency to "thickening of the mitral valve." (Still, the same paper is widely quoted as proving the frequency of mitral stenosis in atrial septal defect.)

A second error in estimating the frequency of Lutembacher's syndrome arises from the study of small numbers of cases. Bedford, Papp, and Parkinson[16] found four cases of Lutembacher's syndrome among ten autopsied cases of atrial septal defect. Taussig and associates[15] reviewed four cases of atrial defect, three of whom had associated mitral stenosis. The small numbers in each of these groups should preclude the use of these excellent publications for purposes of generalization as to the frequency of mitral stenosis with atrial septal defect.

One further point needs to be emphasized. It is well known that the incidence of rheumatic heart disease is higher in people with congenital heart disease than in the average population. Durlacher and Beyer[33] estimate the frequency of rheumatic heart disease in congenital heart disease to be at least 7 per cent, possibly as high as 44 per cent, depending on the criteria used for the diagnosis of rheumatic heart disease. Gelfman and Levine[30] place the incidence at 14 per cent among those with congenital heart disease who live beyond 2 years of age. The same authors state that rheumatic heart disease seems most common in patients with atrial septal defect or bicuspid aortic valves. It may well be possible that a considerable number of clinically diagnosed cases of Lutembacher's syndrome represent in reality rheumatic heart disease with or without mitral stenosis in patients with congenital heart disease.

Finally, our data suggest, as has been asserted repeatedly within the past few years, that congenital mitral stenosis in atrial septal defect patients is extremely rare. None of the sixty patients, mostly infants, with atrial septal defect autopsied at the Children's Hospital showed congenital mitral stenosis. There were only two patients with Lutembacher's syndrome in the Children's Hospital material, both of whom were older children, and the mitral valve involvement was definitely rheumatic in origin.

It seems of considerable importance to us to emphasize the rarity of Lutembacher's syndrome, especially in the light of recent advances in surgical techniques. A great deal of experimental work is being done at this time on surgical closure of atrial septal defects. Obviously, if the probability of mitral stenosis being present at the time of operation, or its development in the future is likely, the wisdom of closing an atrial septal defect may be questioned. On the other hand, and we believe this to be the case on the basis of this study, if the combination of an atrial septal defect with mitral stenosis is quite uncommon, surgical closure of atrial defects should be pursued vigorously.

SUMMARY

1. Apical diastolic murmurs were found in 19 per cent of one hundred consecutive patients with noncyanotic congenital heart disease.

2. Twenty patients with noncyanotic congenital heart disease and apical diastolic murmurs were studied extensively to determine the accurate anatomic diagnosis. Atrial septal defect, ventricular septal defect, and patent ductus arteriosus were the most common lesions found in this series. There was no example of Lutembacher's syndrome in this group of patients.

3. Twenty-five thousand consecutive autopsies studied contained only five cases of Lutembacher's syndrome—representing 6 per cent of all atrial septal defects.

4. Physiologic mechanisms, explaining the origin of these "functional mitral murmurs" in congenital heart disease, are suggested.

5. Diagnostic criteria differentiating the "organic" mitral murmur from the "functional" ones are pointed out.

6. The probability of the development of mitral stenosis in patients with atrial defect is so small that an operation aimed at closure of the defect is highly desirable.

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REFERENCES

1. Duroziez, P.: Essai sur la maladie du coeur: du rhythme pathognomonique du retrecissement mitral, Arch. gen. de med., Paris **20**:385-401, 1862.
2. White, P. D.: A Note on the Differentiation of the Diastolic Murmurs of Aortic Regurgitation and Mitral Stenosis, Boston Med. & S. J. **195**:1146, 1926.
3. Harris, T. N.: Cardiologic Criteria for the Diagnosis of Rheumatic Heart Disease in the Apparently Healthy Subject, Ann. Int. Med. **26**:554, 1947.
4. Evans, W.: Cardiography, St. Louis, 1948, The C. V. Mosby Company, p. 120.
5. Flint, A.: On Cardiac Murmurs, Am. J. M. Sc. **44**:29, 1862.
6. Weinstein, W., and Lev, M.: Apical Diastolic Murmurs Without Mitral Stenosis, Am. Heart J. **23**:809, 1942.
7. Goldstein, B., and Boas, E. P.: Functional Diastolic Murmurs and Cardiac Enlargement in Severe Anemia, Arch. Int. Med. **39**:226, 1927.
8. Robinow, M., and Harger, H. T., Jr.: Functional Mitral Stenosis, Ann. Int. Med. **17**:823, 1942.
9. Taussig, H. B.: Congenital Malformations of the Heart, New York, 1947, The Commonwealth Fund.
10. Louis, P. Ch. A.: Memoires du recherches anatomico-pathologiques, Paris, 1826. Quoted by Brown, J. W.: Congenital Heart Disease, New York, 1950, Staples Press, Ltd.
11. Corvisart, J. N.: Essai sur les maladies et les lesions organiques du coeur, Paris, 1806. Quoted ibid.
12. Lutembacher, R.: De la stenose mitrale avec communication interauriculaire, Arch. d. mal du coeur **9**:237, 1916.
13. Roesler, H.: Interatrial Septal Defect, Arch. Int. Med. **54**:339, 1934.
14. McGinn, S., and White, P. D.: Interauricular Septal Defect Associated With Mitral Stenosis, Am. Heart J. **9**:1, 1933.
15. Taussig, H. B., Harvey, A. M., and Follis, R. H., Jr.: The Clinical and Pathological Findings in Interauricular Septal Defects. A Report of Four Cases, Bull. Johns Hopkins Hosp. **63**:61, 1938.
16. Bedford, D. E., Papp, C., and Parkinson, J.: Atrial Septal Defect, Brit. Heart J. **3**:37 1941.

17. Uhley, M. M.: Lutembacher's Syndrome and a New Concept of the Dynamics of Interatrial Septal Defects, AM. HEART J. **24**:315, 1942.
18. Burrett, J. B., and White, P. D.: Large Interauricular Septal Defect With Particular Reference to Diagnosis and Longevity, Am. J. M. Sc. **209**:355, 1945.
19. Rappaport, M. B., and Sprague, H. B.: The Graphic Registration of Normal Heart Sounds, AM. HEART J. **23**:591, 1942.
20. Jones, J. C., Dolly, F. S., and Bullock, L. T.: The Diagnosis and Surgical Therapy of Patent Ductus Arteriosus, J. Thoracic Surg. **9**:413, 1940.
21. Eppinger, E. C., Burwell, C. S., and Gross, R. E.: Effects of Patent Ductus Arteriosus on the Circulation, J. Clin. Investigation **20**:127, 1941.
22. Levine, S. A., and Geremia, A. E.: Clinical Features of Patent Ductus Arteriosus With Special Reference to Cardiac Murmurs, Am. J. M. Sc. **213**:385, 1947.
23. Ravin, A., and Darley, W.: Apical Diastolic Murmur in Patent Ductus Arteriosus, Ann. Int. Med. **37**:903, 1950.
24. Wood, P.: Congenital Heart Disease. A Review of Its Clinical Aspects in the Light of Experience Gained by Means of Modern Techniques, Brit. M. J. **12**:693, 1950.
25. White, P. D.: Discussion of Paper by Bland, E., and Jones, T. D.: Rheumatic Fever and Rheumatic Heart Disease. A Twenty-year Report on One Thousand Patients Followed Since Childhood, First International Congress of Cardiology, Paris, Sept. 8, 1950.
26. Barber, J. M., Magidson, O., and Wood, P.: Atrial Septal Defect, With Special Reference to the Electrocardiogram, the Pulmonary Artery Pressure, and the Second Heart Sound, Brit. Heart J. **12**:277, 1950.
27. Keith, J. D., and Forsyth, C. C.: Auricular Septal Defect in Children, J. Pediat. **38**:172, 1950.
28. Cosby, R. S., and Griffith, G. C.: Interatrial Septal Defect, AM. HEART J. **38**:80, 1949.
29. Courter, S. R., Felson, B., and McGuire, J.: Familial Interauricular Septal Defect With Mitral Stenosis, Am. J. M. Sc. **216**:501, 1948.
30. Gelfman, R., and Levine, S. A.: The Incidence of Acute and Subacute Bacterial Endocarditis in Congenital Heart Disease, Am. J. M. Sc. **204**:324, 1942.
31. Edwards, J. E.: Personal communication.
32. Brown, J. W.: Congenital Heart Disease, New York, 1950, Staples Press, Ltd., p. 136.
33. Durlacher, S. H., and Beyer, E. C.: The Incidence of Rheumatic Heart Disease in Individuals With Congenital Malformations of the Heart. Abstract of the Scientific Proceedings of the Society, Am. J. Path. **24**:705, 1948.

PHONOCARDIOGRAPHIC DIFFERENTIATION OF VIBRATORY (FUNCTIONAL) MURMURS FROM THOSE OF VALVULAR INSUFFICIENCY: FURTHER OBSERVATIONS AND APPLICATION TO THE DIAGNOSIS OF RHEUMATIC HEART DISEASE

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THE graphic representation of sounds heard over the human precordium has been used not only for teaching purposes and for the permanent recording of such sounds but also as an aid in diagnostic problems encountered in clinical cardiology. In some instances such graphic recording of heart sounds has been suggested to assist the ear of the observer by confirming the presence of suspected murmurs[1-4] and by locating adventitious sounds more accurately in the cardiac cycle, especially in the case of cardiac murmurs.[4-6] The latter application is of particular importance in identifying triple rhythms, when the relative positions in time of the normal and extra heart sounds are of considerable diagnostic importance; a number of studies have been reported of this application.[1,4,7-10]

Phonocardiography has also been applied to the detection or identification of specific cardiac murmurs on which the diagnosis of organic valvular lesions may be based. Thus, diastolic murmurs at the base of the heart or below the left clavicle, inaudible to the ear but visible on heart sound tracings, have in conjunction with audible systolic murmurs provided the evidence necessary for the diagnosis of a patent ductus arteriosus.[4] Again, such tracings have been used by some observers to distinguish presystolic mitral murmurs from roughened or reduplicated first heart sounds and thus give evidence for or against incipient mitral stenosis.[8,11] Finally, phonocardiography has been applied in one instance toward the differentiation of a pathologic from an innocent cardiac murmur in childhood, on the basis of difference in acoustic quality. In 1949 the authors[12] compared phonocardiographic recordings of apical systolic murmurs from known cases of mitral insufficiency due to rheumatic heart disease with similar tracings from other cases of children at whose cardiac apex was audible the nonpathologic vibratory murmur which was described as a "twanging-string murmur" by Still[13] and which has been emphasized by Ash[14,15] as presenting an important diagnostic problem in pediatric cardiology.

The two adventitious sounds were found to yield tracings with characteristically different wave forms: the nonpathologic vibratory murmur appeared as

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a simple wave of constant frequency, such as would be produced by a tuning fork, whereas the murmur of mitral insufficiency appeared as a chaotic mixture of amplitudes and frequencies, such as would be produced by a jet or noise. The clinical importance of the distinction between these two types of murmurs is obvious since not only may the murmur of mitral insufficiency imply a valvular lesion but it is also the most common basis for a diagnosis of rheumatic heart disease or rheumatic carditis, whereas the vibratory or twanging-string murmur is very commonly present in normal children.[16] The latter often occurs in a truly precordial position, with only poor transmission to the apex, and in its most characteristic form is of a quality which can be easily distinguished from the blowing murmur of valvular insufficiency. However, this vibratory murmur may also occur with its point of maximal intensity at or near the apex beat and even be audible beyond that point. Also, it may be of a quality which is difficult to distinguish from that of murmurs of valvular insufficiency, except by those with considerable experience in pediatric cardiology.

In the earlier study, the correlation between phonocardiographic wave form and clinical significance had been supported by clinical data accumulated over a period of some years in the cases of the patients presented. Since the completion of that study further experimental observations have been made, some of which are recorded below. In addition, a number of clinical situations have been encountered by the authors in which the application of this procedure has been of value and, in view of the clinical importance of the distinction between the two murmurs, typical situations of this sort will be briefly presented.

EXPERIMENTAL OBSERVATIONS

1. *Differentiation of the Two Murmurs by Different Instruments.*—It was considered advisable to repeat the comparison of the two types of murmurs with an instrument of different manufacture than that used in the earlier study for two reasons: first, in order to support the significance of the differences observed in the tracings, by showing their independence of the instrument used, and, second, in order to widen the range of application of this difference to diagnostic problems. Accordingly, a number of children with known vibratory murmurs and others with known mitral insufficiency were examined with two instruments, one a Sanborn Stethocardiette (not the same instrument as that used in the earlier study) and the other a Cambridge Stethograph. The tracings obtained with both instruments in two children of each clinical group are shown in Fig. 1. These tracings demonstrate that, whereas small differences can be found between tracings obtained by the respective instruments, each instrument can show the characteristic difference between the wave pattern of the vibratory murmur and that of the blowing murmur of valvular insufficiency.

2. *The Character of the Sound Tracings of Vibratory Murmurs at Points of Diminished Intensity.*—Because of the common occurrence in childhood, both of functional vibratory murmurs and of rheumatic heart disease, it is quite possible to find them coexisting in a given patient. When such a combination involves a vibratory murmur whose point of maximal intensity lies in the midprecordium,

one may find a precordial vibratory murmur with a suspicion or suggestion of roughening into a more blowing character over the apex. In such a case one may find by phonocardiography that in the tracing taken at the midprecordium the wave form of the systolic murmur is of the vibratory type whereas in that taken at the apex the wave form will be smaller and of irregular character.*

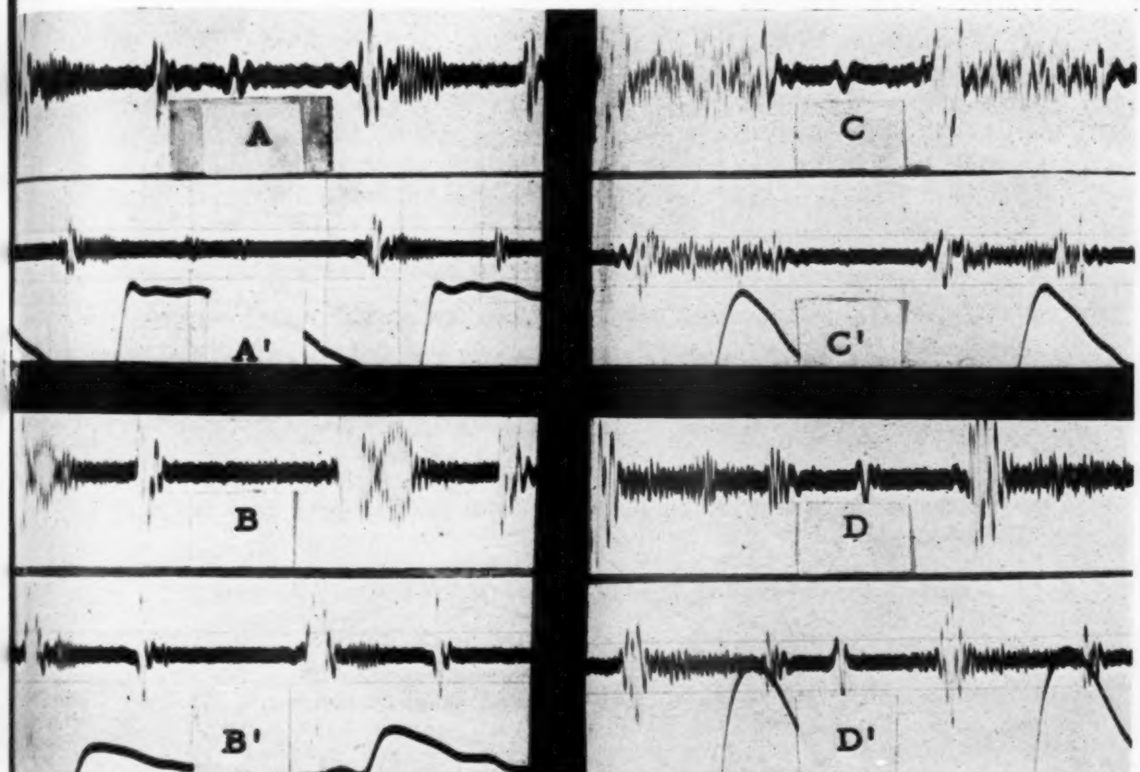

Fig. 1.—Heart-sound tracings as recorded in children with vibratory (functional) murmurs (*A*, *B*) and children with mitral regurgitation (*C*, *D*). Primed letters indicate tracings taken with the Cambridge Stethograph. Companion (unprimed) tracings were taken with the Sanborn Stethocardiette.

In the practical considerations of diagnosis this combination of tracings has raised the following question: does a tracing of lower amplitude and of irregular frequencies and amplitudes at the periphery of a classical vibratory murmur indicate the presence of a second, organic, murmur, or may it represent merely a less distinct form of the vibratory murmur itself, with the regularity of frequency and amplitude marred by transmission through a greater mass of tissue? In order to answer this question, tracings were taken, in the cases of a number of children with pure vibratory murmurs, at the point of maximal intensity of the murmur and at increasing distances from that point, both to the right, until the right sternal border had been passed, and to the left, well into the axilla. The amplification setting of the instrument was kept constant within each such series.

*In combinations involving pronounced mitral insufficiency the transmissions of the blowing murmur into the axilla will make the diagnosis quite clear.

On examining the resultant sets of tracings it was found that the murmur had diminished in amplitude with increasing distance from the point of maximal intensity, but without change in the characteristically regular wave form, until no murmur was visible at all when a sufficient distance had been attained. In no case did the irregularities of frequency and amplitude characteristic of organic murmurs appear, even at the tracing of lowest amplitude. This was true in sets of tracings taken both to the left and to the right. It would appear, then, that the characteristic wave form of the vibratory murmur is not lost throughout the area over which the murmur can be detected by the instruments currently available. Accordingly, a tracing of the "regurgitant" character found at the cardiac apex, at the periphery of an area in which vibratory murmur is detected, should be considered as an indication of a valvular lesion in addition to the functional vibratory murmur.

CLINICAL EXPERIENCE

During the two and one-half years since the earlier study was completed, the authors have observed many patients who illustrate the importance of distinguishing between vibratory murmurs and those of valvular regurgitation. In a considerable number of these cases phonocardiographic tracings were used to assist or confirm the auscultatory findings and of this latter number there were twenty-eight cases in which the tracing showed a wave form characteristic of the vibratory murmur and thus indicated or confirmed the nonpathologic character of the murmur.

These appeared in the following clinical groups:

1. Rheumatic fever with suspected heart disease	3
2. Cardiac murmur noted on routine physical examination by school physicians, with resultant suspicion of rheumatic heart disease	8
3. Fever of unknown origin with cardiac murmur suggesting rheumatic carditis as the diagnosis	13
4. Surgical cases with incidental finding of cardiac murmurs	4
Total	28

Since certain clinical patterns occurred with some frequency, case reports typical of the respective groups are presented.

CASE 1.—*Rheumatic Fever With Suspected Heart Disease.* N. C., a 15-year-old Negro girl, had attended the Rheumatic Fever Clinic of the Philadelphia General Hospital for a period of several years. Her past medical history revealed two hospital admissions associated with acute illnesses diagnosed as rheumatic fever and also a seven-month period of bed rest spent in a convalescent hospital for young cardiac patients. In April, 1943, a heart murmur was discovered during the course of a routine physical examination by a school physician. In October, 1943, the patient was first hospitalized with a diagnosis of rheumatic fever because of a migrating polyarthritis, fever, abdominal pain, and sore throat. At this time a loud systolic murmur was again heard and interpreted to indicate the presence of mitral insufficiency. The erythrocyte sedimentation rate ranged between 20 and 25 mm. per hour through the four months of hospital stay. She was sent directly to a convalescent hospital where she remained for seven more months. Following this presumed episode of rheumatic fever, she was well until April, 1947, when she was

again hospitalized with a diagnosis of acute rheumatic fever because of fever, profuse nosebleeds, and joint pains. A loud systolic murmur was again heard over the entire precordium. The erythrocyte sedimentation rate was 75 mm. per hour (corrected) at the time of this admission, but dropped rapidly to normal within three weeks. Although there was some doubt concerning the degree of rheumatic activity, she was discharged with a diagnosis of rheumatic valvulitis and mitral insufficiency.

Since this last admission, the patient has been followed in the Rheumatic Fever Clinic at the Philadelphia General Hospital for a period of three years. During this interval she has been perfectly well with no symptoms or signs of rheumatic fever or heart disease. On several occasions phonocardiographic tracings were made in an attempt to corroborate the clinical impression held by several members of the clinic staff, that the cardiac murmur audible at present and probably in the past was of a functional or physiologic nature. These tracings showed the characteristic low frequency of vibration and uniform wave pattern indicating a vibratory murmur. The murmur has progressively diminished in intensity during the past three years but still has a low-pitched vibratory quality and on the basis of auscultation alone is clearly a functional murmur. Thus, while this child may have suffered from rheumatic fever, she almost certainly never had rheumatic heart disease with mitral insufficiency. The identification of this murmur as a functional one at an earlier date may well have eliminated a large portion of this child's hospitalization with all of its attending disruptions to normal living and development.

CASE 2.—*Cardiac Murmur Noted on Routine School Examination.* D. A., a 6-year-old Negro girl, was referred to the Rheumatic Fever Clinic of the Philadelphia General Hospital in May, 1948, following the discovery of a loud systolic precordial murmur during a routine school physical examination. There was no family history of rheumatic fever. The patient was afebrile and entirely without complaints. Physical examination in the clinic revealed a moderately loud systolic murmur, low in pitch and vibratory in quality. This murmur was diffusely audible but loudest in the midprecordium just to the right of the apex beat. It could be heard several centimeters to the left of the apex beat but was of diminished intensity in this region. A physiologic third heart sound was present at the apex.

All studies done at the time of the initial clinic visit yielded normal results. These included an electrocardiogram, orthodiagram, erythrocyte sedimentation rate, and streptococcal antihyaluronidase and antistreptolysin determinations. The patient has now been followed for a period of over three years and has developed no evidence of heart disease. She has gained 22 pounds in weight and experienced no illness during this interval. Because of the acoustic quality of this patient's murmur, it has been considered functional in nature. Support for this belief was found in a phonocardiographic tracing which revealed the characteristic slow frequency of vibration and uniform wave pattern of this murmur. The patient has been on unrestricted activity from the start.

CASE 3.—*Fever of Unknown Origin With Cardiac Murmur.* M. H. S., a 5½-year-old white boy, was admitted to the private service of Dr. Joseph Stokes, Jr., at The Children's Hospital of Philadelphia for the study of a fever of undetermined origin. The boy had developed normally and was apparently well until several months prior to admission. During this interval he experienced several "colds" and attacks of sinusitis. Two weeks before hospitalization it was noted that he was listless, easily fatigued, anorexic, and had a low-grade fever. His family physician discovered a loud murmur heard diffusely over the precordium and as far to the left as the anterior axillary line. Two local cardiologists were consulted and concurred in the diagnosis of rheumatic fever with cardiac involvement. The patient was then hospitalized for more extensive study. This revealed no clinical or laboratory abnormalities other than infection of the upper respiratory tract with hypertrophy of the adenoid tissue. Cardiac consultation disclosed a low-pitched systolic murmur with a well-marked musical or vibratory component heard best to the left of the sternum but audible also at the apex and beyond. This was interpreted as a typical physiologic murmur of childhood which could not be used as an indication for the diagnosis of rheumatic heart disease. This interpretation was confirmed by the phonocardiographic tracing which showed a systolic murmur of low frequency of vibration and uniform wave pattern. It was suggested on discharge that the patient would probably benefit from a tonsillectomy and adenoidectomy.

CASE 4.—*Surgical Cases With Incidental Finding of Cardiac Murmurs.* J. L. P., a 9-year-old white girl, was admitted to the surgical service of The Children's Hospital of Philadelphia with the chief complaint of left lower abdominal pain. The clinical picture was not typical of an acute surgical abdomen and operation was delayed for three days. At the end of this interval a mass could be palpated in the left lower abdomen on rectal examination. At operation the left ovary and fallopian tube were found to be hemorrhagic and necrotic due to torsion of these organs. A left salpingo-oophorectomy and an appendectomy were performed without apparent difficulty. The postoperative course was complicated by a temperature elevation to 102.4° F. on the fourth postoperative day. At this time a loud systolic murmur was audible in the midprecordium, the pulse was rapid, and the sedimentation rate was 25 mm. per hour. The diagnosis of rheumatic fever was entertained and a cardiologic consultation requested. The murmur heard was of maximal intensity in the midprecordium and had a low-pitched nonblowing quality. Its functional nature was confirmed by a phonocardiographic tracing which showed the typical uniform wave pattern of the vibratory murmur. The patient's fever and tachycardia subsided spontaneously, with persistence of the cardiac murmur.

SUMMARY

The characteristic difference between heart-sound tracings of murmurs of valvular insufficiency and those of the normally occurring vibratory cardiac murmurs of children can be observed with instruments manufactured by both the Sanborn Company and Cambridge Instrument Company, Inc. The uniform wave form of constant frequency characteristic of the vibratory murmur is seen even in phonocardiographic tracings taken at points distant from that of the point of maximal intensity of that murmur.

Twenty-eight patients with heart murmurs have been catalogued in whom phonocardiographic evidence of a vibratory murmur has suggested or confirmed a clinical decision that the murmur in question was not indicative of heart disease. Case histories typical of these clinical situations have been presented.

REFERENCES

1. Trenberg, H.: Phonocardiography and Its Clinical Correlation, Ann. Int. Med. **14**:1607, 1941.
2. McKee, M. H.: Heart Sounds in Normal Children, AM. HEART J. **16**:79, 1938.
3. Luisada, A. A., and Montes, L. P.: A Phonocardiographic Study of Apical Diastolic Murmurs Simulating Those of Mitral Stenosis, Ann. Int. Med. **33**:56, 1950.
4. Leatham, A.: Phonocardiography, Post-Grad. M. J. **25**:568, 1949.
5. McKee, M. H.: Heart Sounds and Murmurs in Children With Rheumatic Heart Disease, AM. HEART J. **16**:88, 1938.
6. Taquini, A. C., Massell, B. F., and Walsh, B. J.: Phonocardiographic Studies of Early Rheumatic Mitral Disease, AM. HEART J. **20**:295, 1940.
7. Middleton, H. N.: Phonocardiographic Studies on Heart Disease, J. Nat. M. A. **35**:119, 1943.
8. Bartlett, W. M., and Carter, J. B.: Combined Electrocardiography and Cardioscopy in the Early Diagnosis of Heart Disease, Ann. Int. Med. **19**:271, 1943.
9. Luisada, A. A.: Clinical Applications of Phonocardiography, Arch. Pediat. **6**:498, 1943.
10. Koenig, A., and Young, E. W.: The Clinical Value of Heart Sound Tracings With the Electrocardiogram, Pennsylvania M. J. **45**:1279, 1942.
11. Alimurung, M. M., Rappaport, M. B., and Sprague, H. B.: Variations in the First Apical Sound Simulating the So-called "Presystolic Murmur of Mitral Stenosis," New England J. Med. **241**:631, 1949.
12. Harris, T. N., Friedman, S., and Haub, C. F.: Phonocardiographic Differentiation of the Murmur of Mitral Insufficiency From Some Commonly Heard Adventitious Sounds in Childhood, Pediatrics **3**:845, 1949.
13. Still, G. H.: Common Disorders and Diseases of Childhood, ed. 3, London, 1918, Oxford University Press, p. 495.
14. Ash, R.: Evolution of Rheumatic Heart Disease in Childhood, Pennsylvania M. J. **44**:484, 1941.
15. Ash, R.: First Ten Years of Rheumatic Infection in Childhood, AM. HEART J. **36**:89, 1948.
16. Friedman, S., Robie, W. A., and Harris, T. N.: Occurrence of Innocent Adventitious Cardiac Sounds in Childhood, Pediatrics **4**:782, 1949.

THE EFFECTS OF IMPROPER FITTING OF STETHOSCOPE TO EARS ON AUSCULTATORY EFFICIENCY

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THE object of this investigation is to determine quantitatively the effects of leaks at the observers' ears when improperly fitted ear pieces are employed on the binaurals of acoustic stethoscopes.

In a previous communication,[1] we described the instrumentation necessary for measuring stethoscope efficiency at all frequencies in the auscultatory spectrum. Basically, the measuring apparatus is a sound pressure meter which evaluates the sound pressure at the binaural ear pieces of the stethoscope when coupled to artificial ears. The sound pressure which is applied to the artificial ears is expressed in dynes per square centimeter or decibels above a reference such as the average human threshold of hearing. The established threshold reference is equal to 0.000200 dynes per square centimeter.[2]

Data discussed in previous communications[1,3] indicate that the optimal acoustic stethoscope should use binaurals with a $\frac{1}{8}$ inch caliber or bore instead of the usual $^3/_{16}$ inch bore which is common to most all commercially available stethoscopes. The rubber tubing which is interposed between the chest piece and the binaurals should also have a caliber of $\frac{1}{8}$ inch. Furthermore, the tubing should be as short as possible, consistent with convenient handling. Our experience indicates that a rubber tubing length of approximately 10 inches allows adequate maneuverability for most clinical applications. Therefore, a stethoscope with 10-inch rubber tubes was selected in evaluating the effects of leaks at the ears.

Fig. 1 is a graph of our test data which shows the response curve (A) where no leaks are present at the ears. Curve B resulted when a leak was made at the ear which did not have the sound pressure meter connected to it. The magnitude of the leak was a hole 0.015 inch in diameter as compared to a hair diameter of approximately 0.003 inch. It should be kept in mind that the alternate ear is acoustically connected to the ear which has the sound pressure meter connected to it. Curve C results when the alternate ear is well sealed but a 0.015 inch leak is at the ear being measured. Curve D results when a 0.015 inch diameter leak is made at both ears. Curve E results when the alternate ear is disconnected from the artificial ear. The axis of abscissae of the graph is expressed in frequency or cycles per second over the auscultatory spectrum.[3] The axis of ordinates is expressed both in dynes per square centimeter of pressure measured at the artificial ear and the equivalent number of decibels above the average human threshold of hearing.

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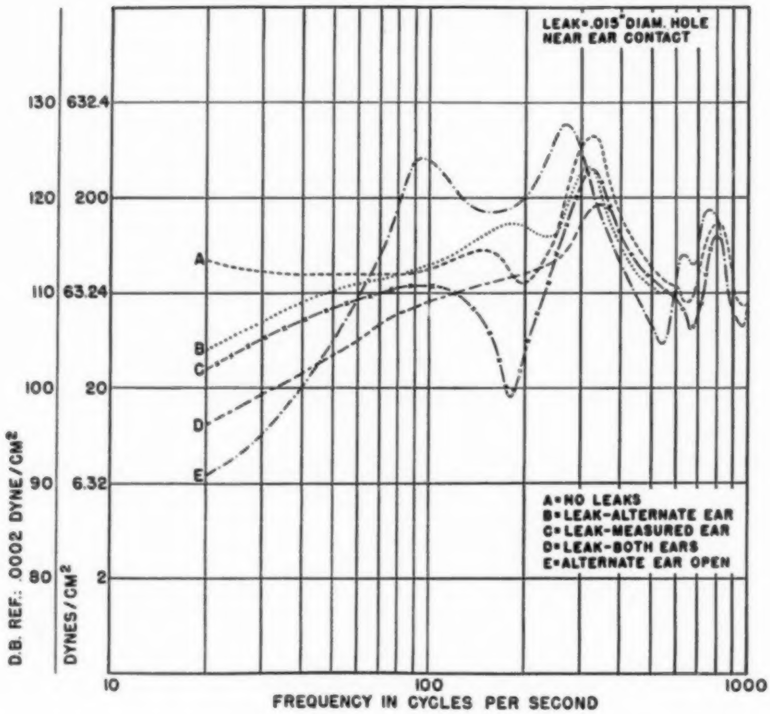

Fig. 1.—Family of frequency response curves of an acoustic stethoscope for various conditions of leak at the binaural ear pieces.

CONCLUSIONS

1. A leak equal to 0.015 inch as has been used in this investigation is a reasonable approximation of what may occur when the stethoscopic ear pieces are improperly fitted. The leak diameter is approximately 5 times the diameter of a single hair.

2. In the very low frequency portion of the auscultatory spectrum from about 70 cycles per second and lower: (a) The maximum stethoscopic efficiency results when no leaks are present. (b) The over-all efficiency of the stethoscope is slightly higher when the leak is in the alternate ear than at the measured car. This phenomenon is of no clinical value but of academic interest only. (c) Leaks of equal size at both ears reduce the efficiency by a marked amount and the efficiency diminishes rapidly as the frequency decreases. (d) The most inefficient condition in the low frequency spectrum results when one of the ear pieces is disconnected from the ear which effectively produces a very large leak.

3. The resonant peaks for the various conditions of leak are altered throughout the auscultatory spectrum.

4. The large leak which occurs when one ear piece is left open to the air improves the apparent efficiency from about 70 to 350 cycles per second. The

effect is nullified by the introduction of excessive room noise which tends to mask the auscultatory sounds. Also, the ability to hear auscultatory sounds with one ear is less than with two ears.[3]

5. Small variance in apparent stethoscopic efficiency occurs between 350 and 1000 cycles per second for all conditions according to measurement. However, a masking effect due to the increased superimposition of room noise upon the auscultatory sounds when leaks are present is most severe in this portion of the auscultatory spectrum.

6. Our quantitative data show that it is imperative to have well-fitted stethoscopic ear pieces for optimal auscultatory efficiency as all types of sounds and murmurs are less well heard when leaks are present.

REFERENCES

1. Rappaport, M. B., and Sprague, H. B.: The Effects of Stethoscope Bore on Stethoscope Efficiency, AM. HEART J. **42**:605-609, 1951.
2. Stevens, S. S., and Davis, H.: Hearing, New York, 1938, John Wiley & Sons, Inc.
3. Rappaport, M. B., and Sprague, H. B.: Physiologic and Physical Laws That Govern Auscultation, and Their Clinical Application, AM. HEART J. **21**:276, 1941.

SOME VIEWS ON THE SIGNIFICANCE OF qR AND QR TYPE COMPLEXES IN RIGHT PRECORDIAL LEADS IN THE ABSENCE OF MYOCARDIAL INFARCTION

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IN RIGHT precordial leads the qR and QR type complexes, in the absence of myocardial infarct, have recently been the subject of several publications.[1-3] The interpretations were quite different and, generally speaking, had little experimental basis. Goldberger[1] attributed these tracings to a considerable rotation of the heart, so that the right precordial points would be facing basal regions of the left ventricle. Kossmann and associates[2] referred the R wave in these complexes to the activation of the "crista supraventricularis." Wilson and associates[3] attributed these complexes to right ventricular hypertrophy which diminished the density of the Purkinje fibers: "qR or QR complexes suggest the hypothesis that the Q wave could be attributed to the decreasing number of unions between the fibers of Purkinje and the muscular fibers of certain areas which would determine some degree of delay of activation at the site of the free wall under the electrode."

To discuss the significance and the origin of these types of tracings, we would like to point out some facts that we believe are firmly established:

1. These tracings are found especially in diseases that produced hypertrophy or dilatation of the right heart chambers, particularly in rheumatic patients with very high-grade mitral and tricuspid valvular lesions (Fig. 7), in acute cor pulmonale (Fig. 18), in chronic cor pulmonale, and in some congenital heart diseases (Fig. 4). It is not surprising, therefore, that Wilson and associates attributed these qR and QR complexes to right ventricular hypertrophy.

2. In right intra-atrial tracings in the normal human heart, similar complexes were obtained (Fig. 1), although with varying relations between the positive and the negative deflections: Qr, QR and occasionally, especially in tracings of the S_1, S_2, S_3 type, complexes of the qR type.

3. The study of right and left intra-atrial tracings[4,5,6] and of epicardial tracings of both atria in the heart of normal dogs reveals the same morphology described in the previous paragraph (Fig. 1).

4. Esophageal[7] and bronchial[8] leads at the level of the left atrium in normal human hearts show similar ventricular complexes and this is suggestive that over the epicardium and within the cavity of the left atrium it is likely that the same potential variations are present as in the dog's heart.

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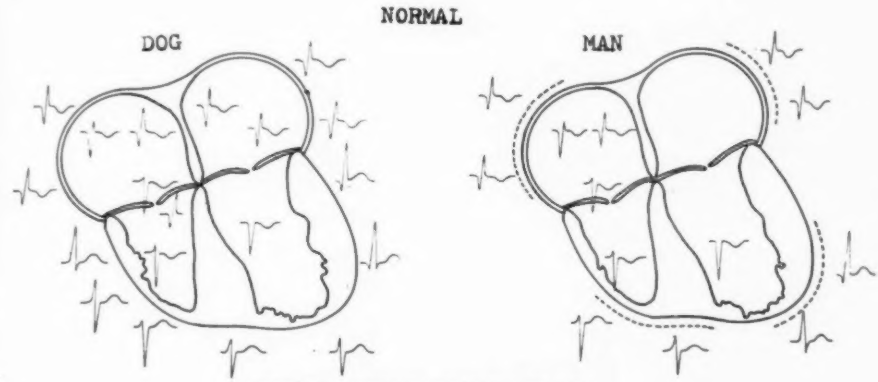


Fig. 1.

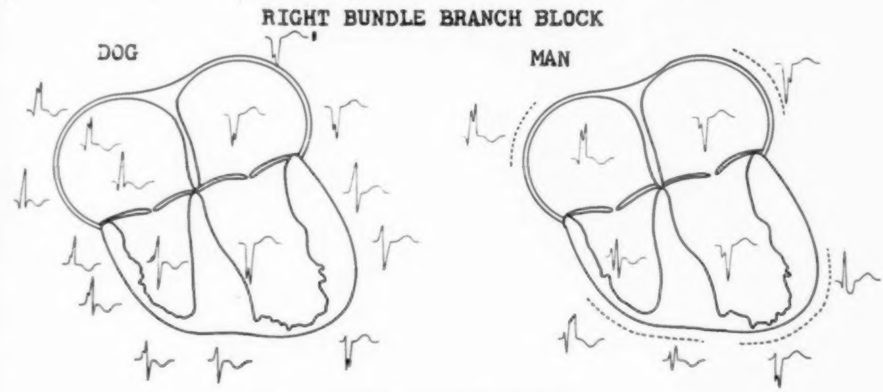


Fig. 2.

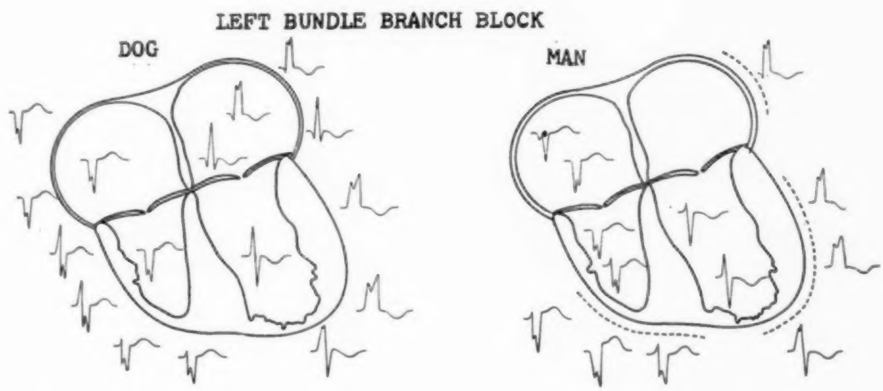


Fig. 3.

Fig. 1.—Morphology of the unipolar leads taken at or near the epicardial surface and within the cavity in the normal hearts of dog and man. The dotted line indicates that the unipolar lead was taken near but not at the epicardial surface, as occurs in the bronchial and esophageal leads.

Fig. 2.—Morphology of the unipolar leads taken at or near the epicardial surface and within the cavity in hearts of dog and man with right bundle branch block. The dotted line indicates that the unipolar lead was taken near but not at the epicardial surface, as occurs in the bronchial and esophageal leads.

Fig. 3.—Morphology of the unipolar leads taken at or near the epicardial surface and within the cavity in hearts of dog and man with left bundle branch block. The dotted line indicates that the unipolar lead was taken near but not at the epicardial surface, as occurs in the bronchial and esophageal leads.

5. Experimental section of the right bundle branch in the dog's heart[5,9] causes the R wave of the QR complex in the right atrium to increase in voltage, to become slurred, and to delay its intrinsic deflection while the Q wave is less negative. The right intra-atrial tracing in the dog becomes qR (Fig. 2). The same takes place in the epicardial tracings of the right atrium. On the contrary, the QR complex of the left atrium, over the epicardium as well as in the cavity, becomes the QS type (Fig. 2). These facts suggest that the late R wave of the right atrium has its origin in some regions of the right ventricle which are activated late in the cardiac cycle.

6. If the left bundle branch is severed experimentally in the dog,[5,9] the R wave of the QR in the left atrium increases in voltage. It also becomes slurred and exhibits a delayed intrinsic deflection. On the contrary the Q wave is less negative. The left intra-atrial tracing of the dog changes to the qR type (Fig. 3). The same is true on epicardial tracings of the left atrium. On the other hand, the QR complex of the right atrium, at the epicardial surface as well as within the cavity, changes to a QS type of tracing (Fig. 3). These facts suggest that the late R wave of the left atrium has its origin in some regions of the left ventricle which are activated late.

7. In cases of right bundle branch block, the intra-atrial tracing in the human heart is quite similar to that recorded in the dog after the experimental section of the right bundle.[5] The tracings obtained are of the qR type with a slurred R wave and a delayed intrinsic deflection (Fig. 2).

8. In cases of left bundle branch block, esophageal tracings recorded at the atrial level in the human heart are very similar to those recorded in and on the left atrium of the dog after the experimental section of the left bundle branch (Fig. 3).

In a patient with interatrial septal defect and right bundle branch block we[6] succeeded in exploring the cavity of the left atrium and obtained the same type of complexes as those recorded from the left atrium of the dog's heart in which right bundle branch block had been produced.

9. Unipolar right limb tracings in normal human hearts often showed the morphology qR or QR, because the right arm faces the right atrium.[6]

10. Usually there are recorded in V_L, when there is a left bundle branch block, complexes of the qR type with slurrings and delays in intrinsicoid deflection.[6]

Consideration of these ten observations has led us to suspect that the findings of qR and QR complexes in V_1 and V_2 etc., are suggestive of exploration of the epicardial surface of the right atrium.

If this is true then it further suggests that the right atrium has been enlarged or the heart has been rotated.

The following cases together with forty-two autopsy reports (four of which are reviewed in some detail) seem to support this view.

CASE REPORTS

CASE 1.—A woman, 50 years old, had congenital heart disease of the cyanotic type, the exact nature of which was obscure. Examination showed a large cardiac outline but no murmurs.

The electrocardiogram showed auricular fibrillation. The standard and unipolar limb leads were suggestive of incomplete right bundle branch block on the basis of slurred and broadened S_1 and the slurred and broadened R in V_R. Very deep Q waves were present in Lead III and V_F, such as occur in some cases of congenital heart diseases (Fig. 4).

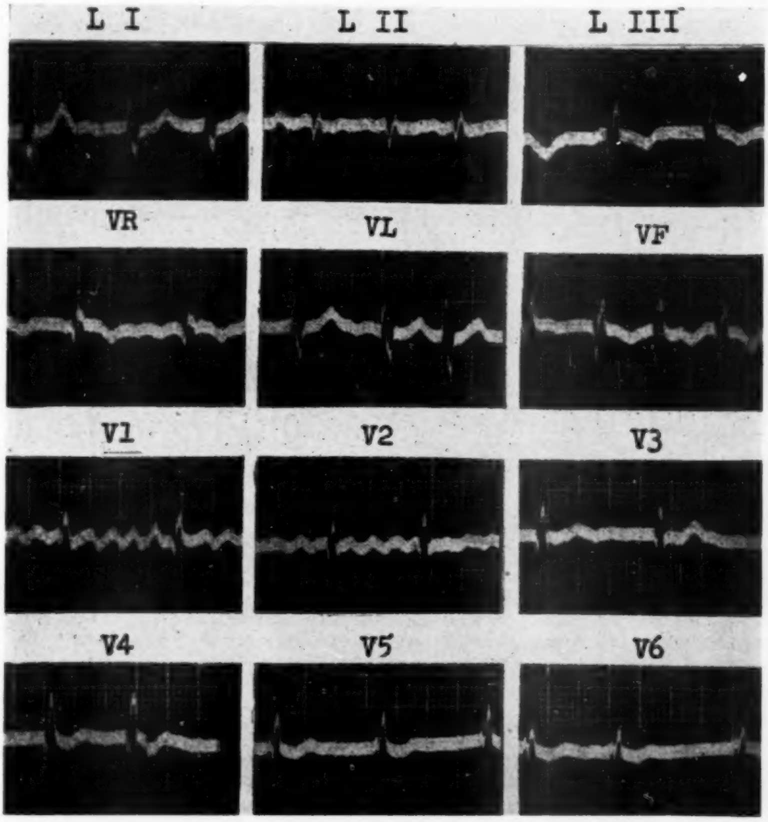


Fig. 4 (Case 1).—Tracing suggestive of incomplete right bundle branch block if we take into consideration the standard and unipolar limb leads (see text). In V_1 and V_4 there are complexes of qR type. In V_2 and V_3 the complexes are of qRs type. In V_5 and V_6 there are M-shaped complexes which could indicate slight incomplete left bundle branch block. The complexes taken from V_1 through V_4 are similar in form to those recorded directly at the epicardial surface or within the cavity of the right auricle in cases of right bundle branch block. This morphology is explained by the great size of the right auricle as was proved in this case.

The precordial leads present most unusual patterns (Fig. 4). In V_1 there is a complex of the qR type; in V_2 and V_3 the complexes are of the qRs type; in V_4 again the qR type and finally in V_5 and V_6 there are M-shaped complexes with rR′. We could not explain this morphology in the precordial leads and so further data were sought.

Catheterization of the right cardiac chambers showed that the greatest part of the area comprising the cardiac outline belonged to the right atrium (Fig. 5), and the tricuspid valve was greatly displaced to the left (*TR*, Fig. 5). The right ventricle was situated beyond this point and quite close to the left border of the heart contour.

With this information the explanation of the precordial electrocardiogram is clarified in that the exploring electrodes in the first four precordial points V_1, V_2, V_3, and V_4 were exploring the right atrium while V_5 and V_6 were opposite the right ventricle. The V_5 and V_6 complexes of right bundle branch block are usually recorded in V_1 and V_2 but had been displaced in this case far to the left by the huge right atrium. Sodi-Pallares and co-workers[4] have described the complexes of the type recorded in V_1 through V_4 in electrocardiograms from the right atrial cavity in the dog and in man and from the surface of the right atrium in dogs in the presence of right bundle branch block.

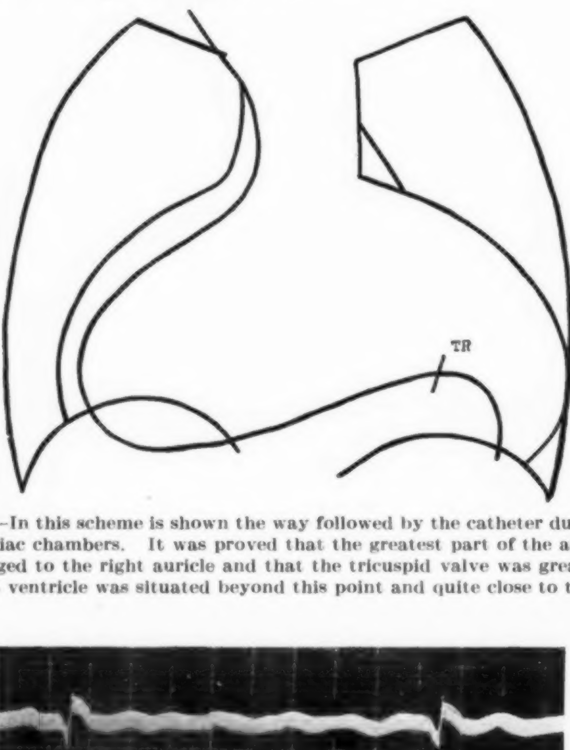


Fig. 5 (Case 1).—In this scheme is shown the way followed by the catheter during the catheterization of the right cardiac chambers. It was proved that the greatest part of the area comprised in the cardiac outline belonged to the right auricle and that the tricuspid valve was greatly displaced to the left (*TR*). The right ventricle was situated beyond this point and quite close to the left border of the heart contour.

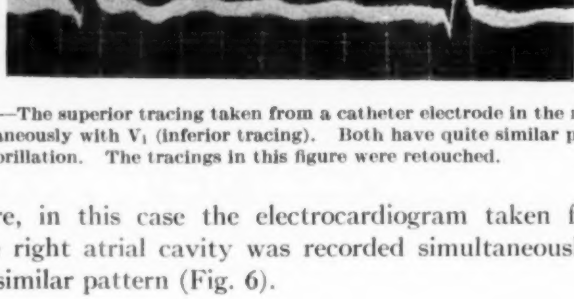


Fig. 6 (Case 1).—The superior tracing taken from a catheter electrode in the right auricular cavity was recorded simultaneously with V_1 (inferior tracing). Both have quite similar patterns (QR). There is auricular fibrillation. The tracings in this figure were retouched.

Furthermore, in this case the electrocardiogram taken from a catheter electrode in the right atrial cavity was recorded simultaneously with V_1 and showed a quite similar pattern (Fig. 6).

CASE 2.—A woman, 33 years old, presented signs of rheumatic mitral stenosis and insufficiency and tricuspid insufficiency and questionable aortic regurgitation.

The electrocardiogram showed auricular fibrillation and the standard and unipolar limb leads were suggestive of right bundle branch block (Fig. 7). In all the six precordial leads, V_1 through V_6, there were complexes of the qR type. We thought that these qR complexes in all precordial Leads V_1 through V_6 indicated right atrial potentials and therefore great enlargement of the right atrium extending to or near to the left border of the heart.

Electrocardiograms taken in a complete circle of the thora as drawn in the outline (Fig. 8) at the level of the fourth intercostal space showed a qR pattern at points *1* and *2* and probably right ventricular pattern, tendency to M complex, at point *5* and probably left ventricular pattern (slurred and broadened S) at points *6*, *7*, and *8*. The circle of the thorax at the level of the fifth intercostal space (Fig. 9) showed qR pattern at points *1* through *4* and right ventricular pattern at points *5* and *6* and questionable left ventricular pattern at point *7*. These electrocardiograms taken around the circumference of the thorax suggested that the left ventricle formed an important portion of the posterior wall of the heart and that the right ventricle also formed part of the same posterior wall, but mainly made up the inferior aspect of the heart.

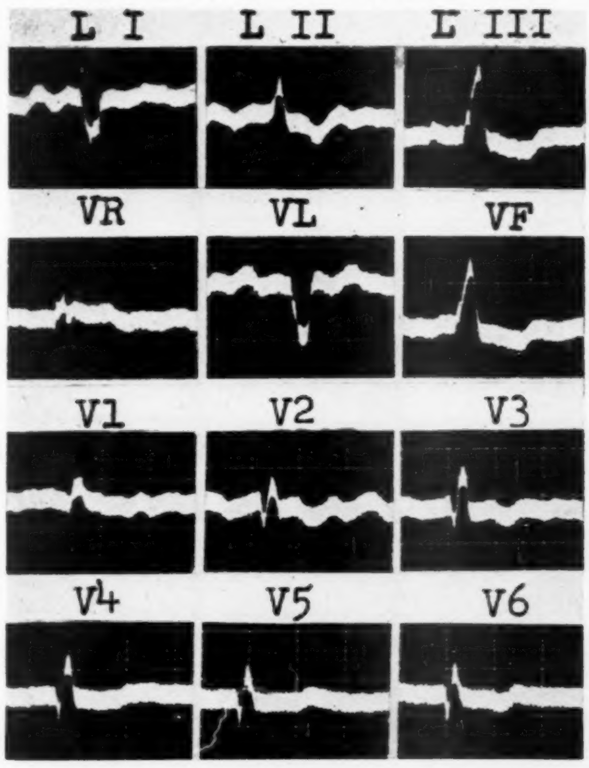
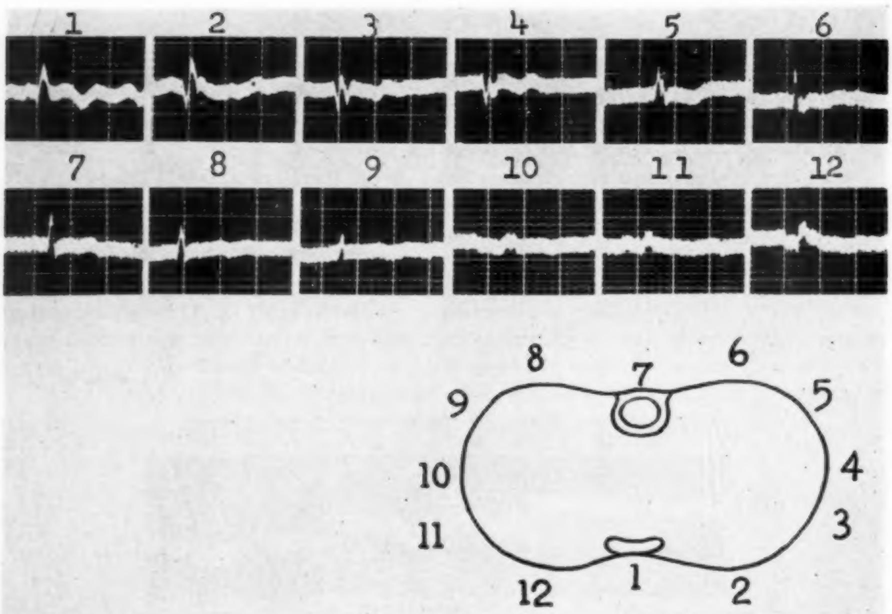


Fig. 7 (Case 2).—There are auricular fibrillation and right bundle branch block. In all the six precordial leads, V_1 through V_6, there are complexes of the qR type.

Teleradiograms in anteroposterior position showed a great dilation to the right, strongly suggesting great right atrial enlargement (Fig. 10). In this anteroposterior film it was impossible to determine how far the right atrium extended to the left.

In order to determine accurately the size of the right atrium and especially to know how closely it approached the left cardiac contour, an angiocardiogram was done. This showed the existence of a very large right atrium lying within the right cardiac contour (this latter was formed by the left auricle) which reached the seventh dorsal upward and advanced to the left to a point slightly inward of the left midclavicular line, without reaching the left cardiac contour (Fig. 11).

Fig. 8.



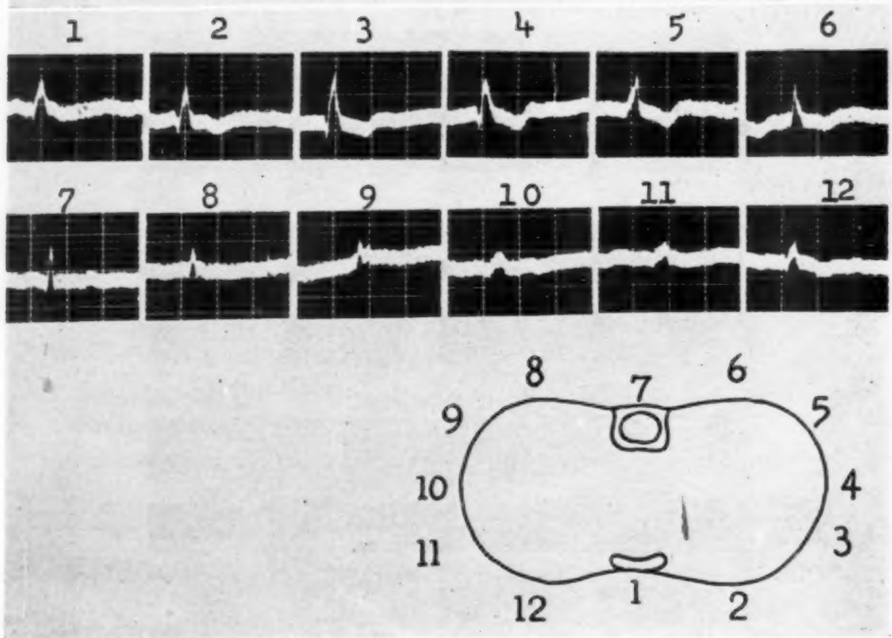


Fig. 9.

Fig. 8 (Case 2).—Electrocardiograms taken in a complete circle of the thorax as drawn in outline at the level of the fourth intercostal space (see discussion in text).

Fig. 9 (Case 2).—Electrocardiograms taken in a complete circle of the thorax as drawn in outline at the level of the fifth intercostal space (see discussion in text).

It seems, from the angiocardiogram, that the right atrium reaches point *4* of the precordial area; nevertheless, complexes of the atrial type are still found in V_5 and V_6. At these leads these complexes still show a right atrial morphology which leads us to believe that the exploring electrode is oriented to the lateral aspect of this atrium.

CASE 3.—A girl, 13 years old, with slight cyanosis was clinically diagnosed as having inter-atrial septum defect with bidirectional flow suggested by catheterization and angiocardiography.

The O_2 saturation of the arterial blood was 76 per cent. After 100 per cent oxygen inhalation, the saturation reached 81 per cent, increasing only 5 per cent, indicating that there was a veno-arterial shunt. The atrial pressure was 2.7 mm. Hg.

The electrocardiogram showed incomplete right bundle branch block with a qR complex in V_1 (Fig. 12). The apex of the R wave was slurred and there was a delayed intrinsicoid deflection. In V_2 and V_3 there was a Rs complex with initial slurring of the upstroke of the R wave. There were also broad slurred S waves in Leads I, V_5, and V_6.

The diagnosis of right atrial dilatation was made on the basis of the qR in V_1.

This diagnosis was substantiated by the angiocardiographic study which showed an enlarged right atrium (Fig. 13). The diodrast immediately filled the right atrium and was probably prevented or delayed from passing to the left atrium by the higher pressure in the left atrium at the moment.

CASE 4.—A woman, 47 years old, had mitral stenosis and insufficiency and heart failure. On examination there was a greatly enlarged heart and the characteristic mitral murmurs.

The electrocardiogram showed auricular fibrillation and incomplete right bundle branch block with a QRS of 0.11 second (Fig. 14). In V_1 there was a qR complex with a slurred R apex and late intrinsicoid deflection. In V_3 there was a qRs. On the basis of these findings in V_3 with those of V_1 the diagnosis of dilatation of the right atrium was made.

The teleradiogram showed a large heart with an arc to the right indicating great right atrial dilatation (Fig. 15).

REPORTS OF CASES WITH NECROPSY

CASE 5.—A woman, 45 years old, presented the clinical findings of mitral stenosis and insufficiency and tricuspid insufficiency.

The electrocardiogram showed (Fig. 16) right axis deviation ($\hat{A}_{QRS}$ in + 120 degrees). The P wave was peaked in Leads I and II, diphasic in V_1. There was a qRs complex with a negative T wave in V_1. Lewis's index was — 18 mm. We thought that the tracing suggested right atrial hypertrophy by the presence of qRs complex in V_1 and the peaked P waves in Leads I and II.

Autopsy Report.—The heart was totally enlarged, especially its right cavities. The right atrium was greatly dilated and also the left atrium. The right ventricle was large and much greater than the left one. Its wall measured 9 mm. in thickness. The mitral valve measured 45 mm. circumference. Its valves were fused forming a rigid diaphragm with partial calcification. The tricuspid valve had its tendons shortened and its valves were thick and showed fibrinous verrucae of rheumatic nature. The aortic valve was normal.

CASE 6.—A woman, 56 years old, had the clinical signs of mitral stenosis and insufficiency and probably tricuspid insufficiency. The patient was in heart failure.

The electrocardiogram (Fig. 17) showed right axis deviation ($\hat{A}_{QRS}$ in + 140 degrees) and auricular fibrillation. There was a qR complex with negative T wave in V_1. We thought that the tracing suggested hypertrophy of the right cavities, mainly of the right atrium.

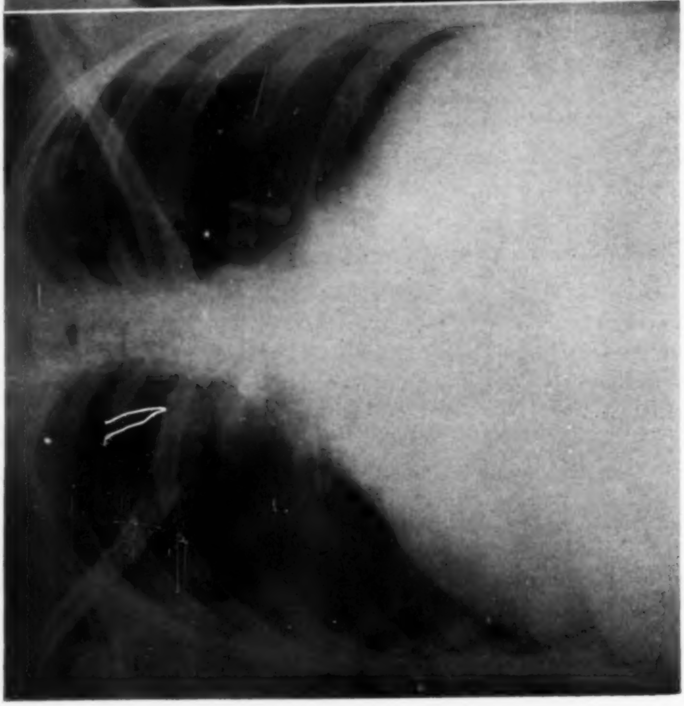


Fig. 10.

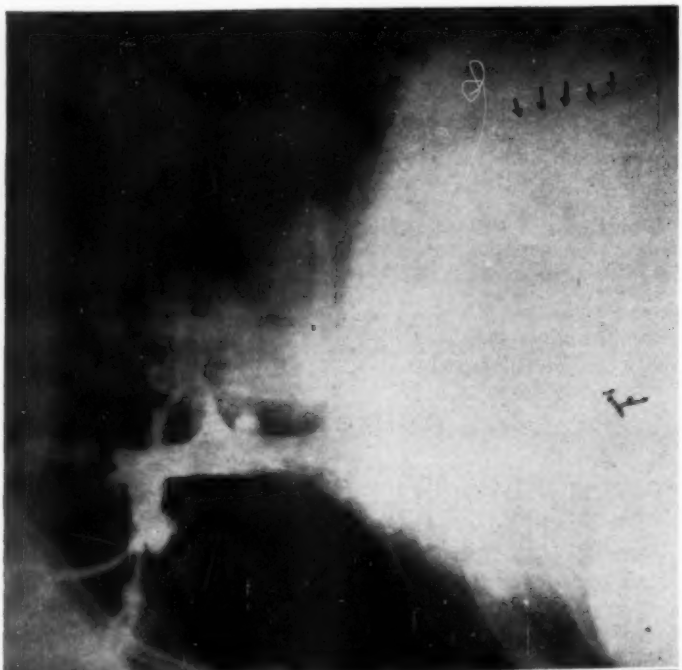
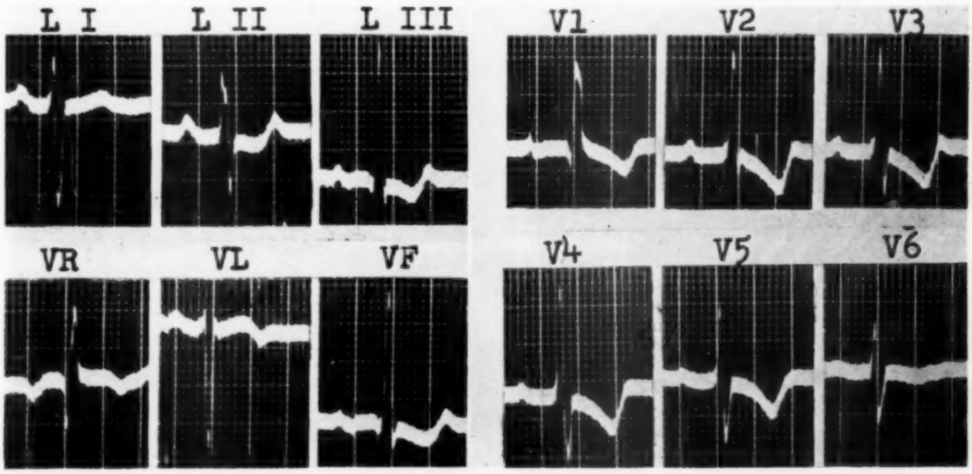


Fig. 11.

Fig. 10 (Case 2).—Teleradiogram in anteroposterior position showing a great dilatation to the right strongly suggestive of great right auricular enlargement.

Fig. 11 (Case 2).—Angiocardiogram showing the existence of a very large right auricle lying within the right cardiac contour (this latter was formed by the left auricle). The left border of the right auricle is indicated by small arrows.

Autopsy Report.—The heart was totally enlarged, especially its right cavities. The right atrium was greatly dilated. The left atrium was also increased in size. The mitral valve was not recognizable, since its cusps were completely fused, very thick and in some parts calcified, with the chordae tendineae almost entirely obscure. It had the shape of a straight and rigid funnel. The tricuspid valve leaflets were slightly shortened and thickened at their free edge, which showed some rheumatic verrucae.



A. *B.*

Fig. 12 (Case 3).—There is incomplete right bundle branch block with a qR complex in V_1 which suggests right auricular dilatation.

Fig. 13 (Case 3).—Angiocardiographic study which showed an enlarged right auricle.

Case 7.—A woman, 45 years old, was found to have the clinical evidence of pneumonia produced by Friedländer's bacillus and pneumococcus. An acute cor pulmonale was also diagnosed.

The electrocardiogram (Fig. 18) showed an S_1, S_2, S_3 type of tracing with QR complexes in Leads V_1 and V_2. Slurring of S in left precordial leads and of R in lead V_R were suggestive of incomplete right bundle branch block. There was a markedly positive RS-T displacement in the right precordial leads. There was a negative displacement of RS-T in V_5 and V_6. The tracing was interesting because of the morphology in V_1 and V_2 which might lead to a diagnosis of a recent anteroseptal myocardial infarction. Yet it was difficult to admit that a recent infarct with injured areas should only be present in V_1 and V_2 because the infarcts localized to the right ventricle are exceptional.

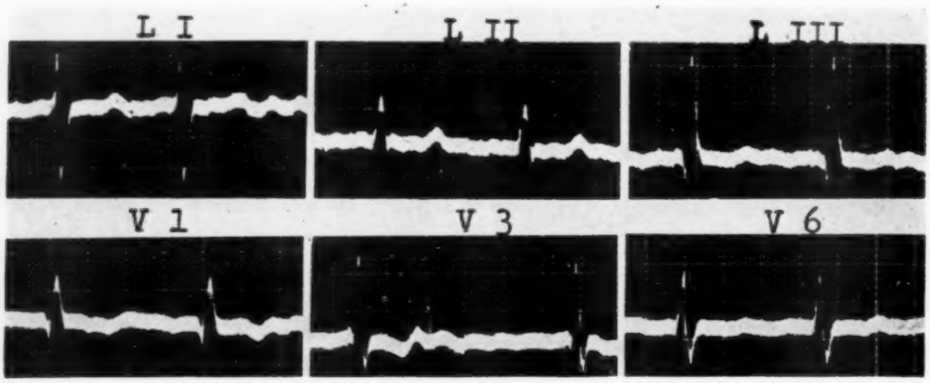


Fig. 14 (Case 4).—This tracing shows auricular fibrillation and incomplete right bundle branch block. In V_1 there is a qR complex suggestive of right auricular enlargement.

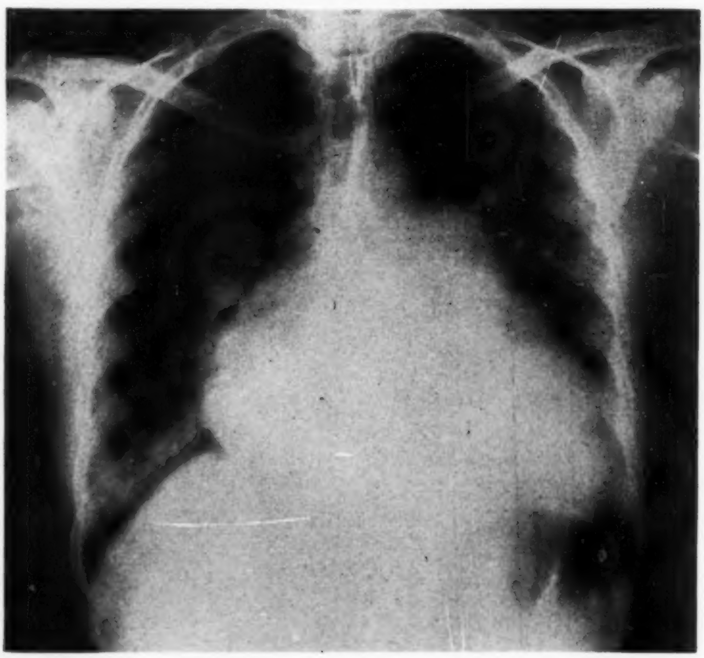


Fig. 15 (Case 4).—Teleradiogram showing a very large heart with a great arc to the right, indicating great right auricular dilatation.

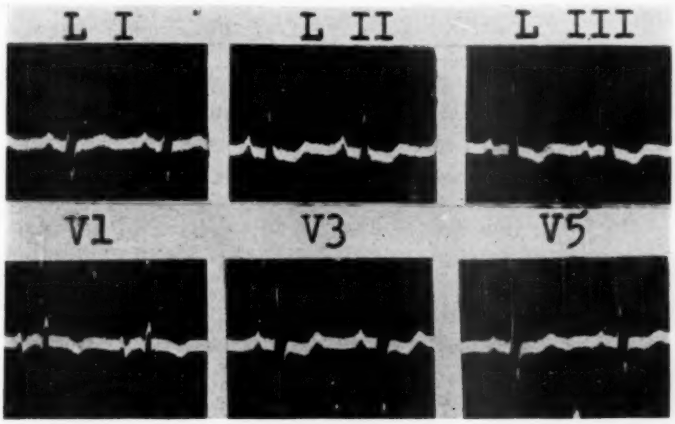


Fig. 16 (Case 5).—In this tracing there is a qRs complex with negative T wave in V_1 suggesting right auricular enlargement.

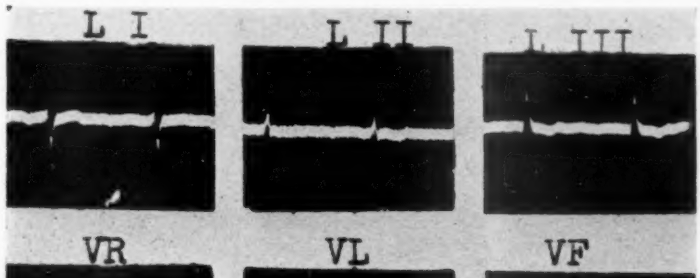


Fig. 17 (Case 6).—This electrocardiogram shows right axis deviation and auricular fibrillation. There is a qR complex with negative T wave in V_1, suggestive of right auricular dilatation.

Zuckermann and associates[10] have stated, on the other hand, that acute cor pulmonale may give this type of tracing. In fact, this tracing was published by this author. Should it not be a myocardial infarction, the tracing suggested a great right atrial dilatation and the presence of myocardial injury on the epicardium of the free wall of the right ventricle[10] or over the right septal surface.[10] In other words, the tracing is compatible with and is even suggestive of acute cor pulmonale.

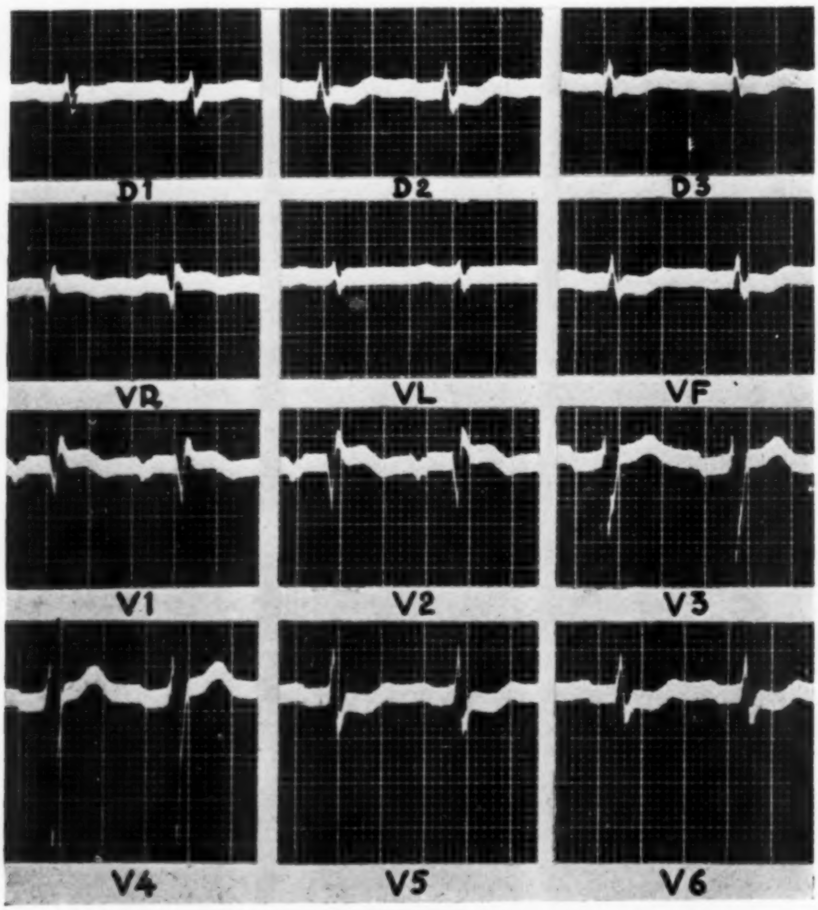


Fig. 18 (Case 7).—This tracing shows QR complexes with marked RS-T displacement in V_1 and V_2. There is a negative displacement of RS-T in V_5 and V_6. These changes may lead to a diagnosis of a recent anteroseptal myocardial infarction. The necropsy study did not show myocardial infarction. The right auricle was very large (see discussion in text).

Autopsy Report.—The heart was enlarged, especially the right cavities. The right atrium was very large. The ventricle was also large and had a thick wall. The left cavities were normal in size. The left lung had a cavity at the apex, the size of a cantaloupe. At some portions there were membranous-like formations which were easily detached. The adjacent parenchyma had a blackish-gray color and was soft. In the rest of the lung there was pus and bloody fluid.

Diagnosis.—Acute cor pulmonale. Atypical lobar pneumonia of the left lung. There was no myocardial infarction.

CASE 8.—A girl, 16 years old, had the clinical findings of mitral stenosis and insufficiency and tricuspid stenosis and insufficiency and heart failure.

The electrocardiogram (Fig. 19) showed auricular fibrillar-flutter. $\hat{A}_{QRS}$ was + 110 degrees with probable incomplete right bundle branch block if the slurred S wave in Lead I and V_5 were considered. There was also a qR complex in V_1 which led us to believe that there was great right auricular dilatation. The tracing was also suggestive of right ventricular hypertrophy.

Autopsy Report.—The heart was small (260 grams) and could be moved freely within the chest. The right atrium was very much enlarged. The right ventricle was small. Its wall measured 2 mm. in thickness, and in some sites it was merely thin scar tissue. The tricuspid valve measured 25 mm. in circumference and 7 mm. in diameter. It was a funnel-shaped thin fibrous inextensible diaphragm.

The left atrium was dilated. The mitral valve appeared similar to the tricuspid but the chordae tendineae were thicker and shortened. It had a diameter of 10 millimeters.

Diagnosis.—Marked tricuspid stenosis with slight tricuspid regurgitation due to the inextensibility of the valve and a double mitral lesion.

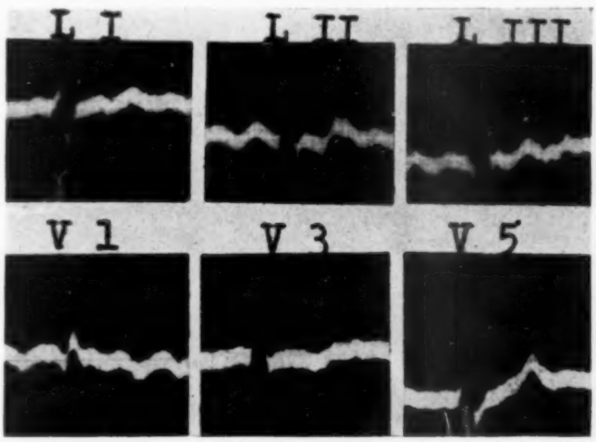


Fig. 19 (Case 8).—There is auricular fibrillation and right bundle branch block. The qR complex in V_1 suggests a great right auricular dilatation.

Tables I and II summarize the data which in our estimation are the outstanding features in the forty-two autopsy reports.

TABLE I

DIAGNOSIS	NO. OF CASES
Double mitral lesion	3
Pure mitral stenosis	1
Double mitral lesion plus double tricuspid lesion	11
Double mitral lesion plus tricuspid regurgitation (in 3 there was an added aortic lesion)	19
Chronic cor pulmonale (3 due to pulmonary emphysema; 2 to kyphoscoliosis)	5
Acute cor pulmonale (result of Friedländer's pneumonia)	1
Cor triloculare biventricular plus aortic coarctation	1
Cor biloculare with pulmonary stenosis and transposition of the great vessels	1

DISCUSSION

In this paper we have stated that we were recording in precordial leads V_1 and V_2 almost the same variations of potential that are present at the epicardial surface of the right atrium and we know also that in general quite similar variations exist on the endocardial as on the epicardial surface at a given point in the right atrium. Here we have referred sometimes to the pattern as representing either endocardial or epicardial variations of potential.

TABLE II

RIGHT ATRIUM

DILATATION	NO. OF CASES
+	1
+ +	19
+ + +	15
+ + + +	7

RIGHT VENTRICLE

HYPERTROPHY OR DILATATION	NO. OF CASES
+	3
+ +	19
+ + +	14
+ + + +	5
There was 1 case of single ventricle.	

LEFT ATRIUM

DILATATION	NO. OF CASES
+	8
+ +	19
+ + +	7
+ + + +	2
Dilatation was present in 36 cases.	

LEFT VENTRICLE

HYPERTROPHY OR DILATATION	NO. OF CASES
+	16
+ +	8
+ + +	3
+ + + +	1
Hypertrophy or dilatation in 28 cases.	

We state this in the face of the recent claims in certain papers on vectorcardiography[11,12] that insist that the variations of potential at a precordial electrode cannot be referred to the surface potentials of the part of the heart adjacent to the exploring area on the chest wall. They state that the variations of potential of the precordial electrode represent the resultant of all of the cardiac vectors of the heart that are correctly oriented toward the given precordial electrode.

This statement is correct yet not in contradiction to our views for the following theoretical and experimental reasons.

Wilson[6,13] has established by application of the Poisson integral that the resultant of all the vectors produced in the heart (Integral of Volume) is equivalent to the resultant of all the vectors in the surface (Integral of Surface).

A unipolar lead registered on the epicardium or at a distance from the heart will be directly proportional to the electric moment of all the vectors considered on the surface. In fact, in the unipolar tracings registered on the epicardium, both the ascending branch of R and the terminal branch of S are described as extrinsic phenomena and the corresponding electrical changes produced at a distance from the recording electrode—at least from the theoretical point of view—may be referred to surface vectors also distant from the exploring electrode. As we have experimentally withdrawn the electrode to varying distances from the surface of the heart, the changes in the tracing appear to us minimal and unimportant for practical purposes. These slight changes (mainly in the time of the intrinsicoid deflection and not in the morphology of the tracing) are the result of the distance since the potential varies inversely as the square of the distance in the volume integral and inversely as the cube of the distance in the surface integral.

The advantages derived from this analysis of Wilson are great and of immediate practical value for, if we know the morphology of the curves taken from the surfaces of the atria and ventricles in normal and pathologic conditions, we have an idea of the position of the heart and if and where there are existing abnormalities.

The other support of this idea comes from the experimental work done on dogs.

Wilson and co-workers[14] have demonstrated the great similarity of curves taken directly from the heart and those taken from the precordial region. In the normal dogs the curves taken from the trabecular portion of the right ventricle were similar to those taken from the precordium or chest wall in positions corresponding to V_1 and V_2. The tracing taken from the anterior and lateral aspects of the left ventricle were the same as those recorded in positions V_5 and V_6. Those curves taken from the anterior septal region which were transitional in shape were similar to those recorded in positions on the precordium corresponding to V_3 and V_4.

Ferrero and co-workers,[15] using a special technique of precordial transfixion in the dog, compared the curves taken at various depths and found that the morphology was practically the same if the transfixing electrode was maintained

in the line perpendicular to the surface of the heart. The only important differences were moderate changes in the time of the intrinsic deflections.

In Case 1 we have recorded very similar tracings taken simultaneously from the cavity of the right atrium and from the precordial position V_1.

In all of this we have not considered the qR to be a complex of atrial origin. It is definitely a ventricular complex but we are recording it through and from the right atrium. The problem was to determine the origin of the qR complex which Goldberger[1] had referred to the left ventricular base and Kossmann and associates[2] had attributed to the activation of "crista supraventricularis" in the right ventricle.

By a special technique previously described,[16] we have recorded Qr and QRs complexes experimentally in dogs from the right upper portion of the interventricular septum. This part of the right septum is normally activated late in the cardiac cycle. The application of very close contiguous bipolar electrodes have shown the intrinsic deflection to be late and corresponding to the downstroke of the R in the unipolar lead. To explain the initial negativity or q at a point where the wave of depolarization is approaching, it is necessary to consider that there are other vectorial forces that withdraw from the explored site, which are of greater magnitude than those that correspond to the activation wave which approaches the exploring electrodes. This is possible if it is considered that the septal muscular portion of the right ventricle through which the activation wave approaches is very thin, and that all the activation vectors of the free ventricular walls belong to considerably thicker muscular portions.

When the activation process is very close to the exploring electrode, it will determine a greater positivity which is variable according to the orientation and magnitude of the distant vectorial forces.

Experimentally in dogs in which right bundle branch block has been produced, we[9,16] have recorded from the right upper ventricular septum and from the right atrial cavity two types of complexes: qR type with broad slurred R and late intrinsic deflection and qRs very similar to the complex that appeared in V_2 and V_3 in the first case (Fig. 4).

This strongly suggests that when we are recording QR complexes from the right precordium the exploring electrodes are facing the right upper ventricular septum through the dilated right atrium. Furthermore, this concept agrees with the facts delineated in paragraphs 1 to 10 establishing that the R wave is produced by some portions of the right ventricle that are activated late.

Since QR complexes have also been recorded from the left atrium there exists the suggested possibility that qR complexes may exist in the upper left septum which has not yet been adequately explored.

The previous ideas imply that the surrounding environment of the heart is homogeneous and does not greatly modify the distribution of the electrical currents. There may be found local changes in this environment that change the distribution of the potentials, but the experiments pointed out previously lead us to believe that these changes are not significant. Since to the present time we do not know the extent to which the potential variations should be corrected, we do not believe it is practical to consider these factors until more experimental evidence is secured.

Kossmann's idea is quite similar to ours, since the "crista supraventricularis" belongs to the interventricular septum at its higher levels. In Fallot's tetralogy, qR complexes are commonly found over the right precordial leads with a very large R wave. One should not forget that in this disease there is an infundibular stenosis with a considerable hypertrophy of the muscular portion belonging to the "crista supraventricularis" that may determine the great voltage of R over the right precordial leads.

It is difficult to accept Goldberger's views. It is furthermore impossible to accept the idea that the base of the left ventricle might be oriented to Leads V_1 through V_4 in Case 1, and to V_1 through V_6 in Case 2.

SUMMARY

1. It is considered that qR and QR complexes in right precordial leads in the absence of myocardial infarction are a good indication of right atrial dilatation.

2. This statement was proved in cardiac cases wherein the right cavities were affected. It was furthermore proved by angiocardiography and necropsy studies that the right atrium was enlarged.

3. The similarity of differences of potential recorded at the atrial surface and within the cavity are pointed out by means of the intra-atrial leads in man and in the dog, by atrial epicardial leads in the dog, and by esophageal and bronchial leads in man.

4. Since the same potentials were found over the epicardial surface of the right atrium and within its cavity, qR and QR complexes were registered both at these sites and over the right precordial leads. It was believed the potential was registered very close to the surface of the right atrium. This implies that this atrium was enlarged, in order to approach points C_1 and C_2 or that a rotation of the heart took place in such a way as to approximate the right atrial wall to the chest wall.

5. These complexes (qR and QR) have been found experimentally in high portions of the interventricular septum which have a delayed activation. When they are registered over the right precordial leads it is probable that the exploring electrode is oriented to these aspects of the septum through the dilated right atrium.

REFERENCES

1. Goldberger, E.: The Differentiation of Normal From Abnormal Q Waves, AM. HEART J. **30**:341, 1945.
2. Kossman, Ch., Berger, A. R., Rader, B., Brumlik, J., Briller, S. A., and Donnelly, J. H.: Intracardiac and Intravascular Potentials Resulting From Electrical Activity of the Normal Human Heart, Circulation **2**:10, 1950.
3. Wilson, F. N., Rosenbaum, F. F., and Johnston, F. D.: Interpretation of the Ventricular Complex of the Electrocardiogram, Advances Int. Med. **2**:1, 1947.
4. Sodi-Pallares, D., Thomsen, P., Soberón, J., Fishleder, B. L., Estandía, A., and Barbato, E.: El Electrocardiograma Intracavitario Humano, Ed. Inst. Cardiol. México, 1948.
5. Sodi-Pallares, D., Viscaíno, M., Soberón, J., and Cabrera, E.: Comparative Study of the Intracavitary Potential in Man and in Dog, AM. HEART J. **33**:819, 1947.
6. Sodi-Pallares, D.: Neuvas Bases de la Electrocardiografía, ed. 3, Ed. Inst. Natl. Cardiol. México, 1951.
7. Kistin, A. D., Brill, W. D., and Robb, G. P.: Normal Esophageal and Gastric Electrocardiograms. Description, Statistical Analysis and Bearing on Theories of "Electrocardiographic Position," Circulation **2**:578, 1950.

8. Zuckermann, R., Bisteni, A., and Ortiz, J.: Derivaciones Bronquiaies, Arch. inst. cardiol. México **20**:387, 1950.
9. Sodi-Pallares, D., Thomsen, P., Barbato, E., Soberón, J., Fishleder, B. L., and Estandía, A.: Bloqueos Incompletos de Rama, Arch. inst. cardiol. México **18**:497, 1948.
10. Zuckermann, R., Rodríguez, M. I., Sodi-Pallares, D., and Bisteni, A.: Electropathology of Acute Cor Pulmonale, Am. Heart J. **40**:805, 1950.
11. Duchosal, P. W., and Sulzer, R.: La Vectocardiographie, Suisse, 1948, S. Karger.
12. Scherlis, L., Lasser, R. P., and Grishman, M.: Spatial Vectorcardiography: The Normal Vectorcardiogram. VI, Am. Heart J. **42**:235, 1951.
13. Wilson, F. N.: On the Choice of a Reference Point for the Study of the Electrical Field of a Tissue Immersed in a Volume Conductor, Libro Homenaje al Prof. Ignacio Chávez. México, 1945.
14. Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., Erlanger, H., Kossmann, C. E., Hecht, H., Cotrim, N., Menezes de Oliveira, R., Scarsi, R., and Barker, P. S.: Am. Heart J. **27**:19, 1944.
15. Ferrero, G., Duchosal, P. W., Doret, J. P., Grosguerin, J., and Mastrangelo, E.: Comparaison entre dérivations épicardiques et précordials. Read at First International Congress of Cardiology in Paris, 1950.
16. Sodi-Pallares, D., Rodríguez, M. I., Chait, L. O., and Zuckermann, R.: The Activation of the Interventricular Septum, Am. Heart J. **41**:569, 1951.

THE EFFECT OF ECCENTRICITY ON SPATIAL VECTOR ANALYSIS OF THE ELECTROCARDIOGRAM OF THE NEWBORN INFANT AND ON THE CORRELATION BETWEEN THE ELECTROCARDIOGRAM AND THE VECTORCARDIOGRAM

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AN IMPORTANT cardiological problem in the newborn infant is the diagnosis of abnormal right ventricular hypertrophy, for it occurs often in congenital heart disease. Unfortunately, the electrocardiogram taken during the first few weeks of life cannot contribute much clinically to the solution of this problem.

The normal neonatal record is already one of right preponderance[1]; it appears to be impossible to differentiate abnormal from normal right preponderance when only a single record is available. As demonstrated by one of us,[2] the only way to diagnose pathologic right preponderance in the newborn infant is by comparison of serial tracings taken over a period of weeks and months. Normally the degree of right preponderance decreases with age; if serial tracings show an increase, abnormal right preponderance is indicated.

Attempts have been made to establish the normal range of right preponderance by determining the normal values for times of onset of intrinsicoid deflections, QRS voltages, and R/S ratios in the chest leads.[3,4] These standards were intended to permit the recognition of a greater than normal degree of right preponderance. To our knowledge this has not been successful; no case has been reported where a diagnosis of abnormal right preponderance has been made in the newborn infant from a single tracing.

Two recent developments promise to aid in the solution of the problem. Vectorcardiography, the direct registration of the spatial vector loops, appears capable of differentiating the abnormal from the normal right preponderance in the older age groups.[6,7] Whether this will also hold for the neonatal period remains to be seen. A second development has been spatial vector analysis of the electrocardiogram according to the method of Grant.[5] This procedure determines the mean spatial vector of the QRS complex by means of the routine limb and chest leads. Since it has been of considerable value in the diagnosis of right preponderance in the adult, we felt that an investigation of its possibilities in the newborn infant might be worth while.

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The infants utilized in this study were from the Pediatric Service (Dr. Lawrence B. Slobody, Director).

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A few ordinary tracings of newborn infants were recorded; they included the six limb leads, V_{6R}, V_{4R}, $V_{STERNUM}$, V_4, V_6, and a few unipolar leads from the back. Upon applying Grant's method of vector analysis to such tracings, several serious discrepancies were noted, sufficient to cast doubt on the validity of the method for the neonatal record. Then we proceeded to take many leads which systematically covered the entire chest, as will be described below.

METHOD

Electrocardiographic studies were obtained on six normal infants, 3 to 10 hours old; in one of these a second series was recorded three days later. Infant type electrodes and a single channel direct-writing machine were employed. After recording the standard bipolar and augmented unipolar limb leads, the chest was explored with fifty-six unipolar leads in accordance with the following scheme. In each of the ten following lines five leads were taken: right anterior axillary, right midclavicular, sternal, left midclavicular, left anterior axillary, left posterior axillary, left scapular, vertebral, right scapular, and right posterior axillary. Each of these lines extended from the level of the clavicle to the level of the tenth rib. In the midaxillary line on each side three leads were taken. Fig. 1 shows the distribution of the leads.

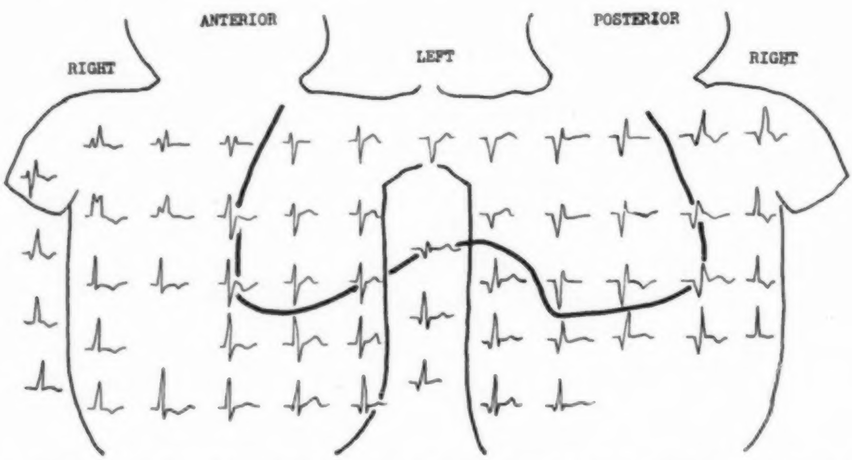

Fig. 1.—Newborn girl, 9 hours old. Diagram of the distribution of the QRS complexes on the chest. The contours of the complexes were copied from the original electrocardiogram without any regard for the amplitudes of the deflections. Only the relative sizes of the positive and negative waves were observed so that a given complex could be designated as positive, negative, or transitional. The heavy line is the transitional zone. It divides the chest into positive and negative sections. It defines a plane which is almost vertical and slightly tilted from the left anteriorly to the right posteriorly. The plane is located near the left shoulder. The spatial vector of the QRS complex, which is perpendicular to this plane, is almost horizontal and points slightly anteriorly. Its center, which is located somewhere on the plane, is located close to the left shoulder, and it seems to lie more to the left than the center of the ventricular mass.

The QRS complexes were copied onto a diagram of an infant's chest. Little attention was paid to the amplitude of the deflections, since the evaluation concerned the polarity alone. The positive and negative areas in each complex were measured and added so that each complex as a whole could be characterized as

positive, negative, or transitional. The last type consisted of equal parts of positivity and negativity. No attempt was made to analyze the P and ST-T complexes because of their small size and lack of definition in many leads.

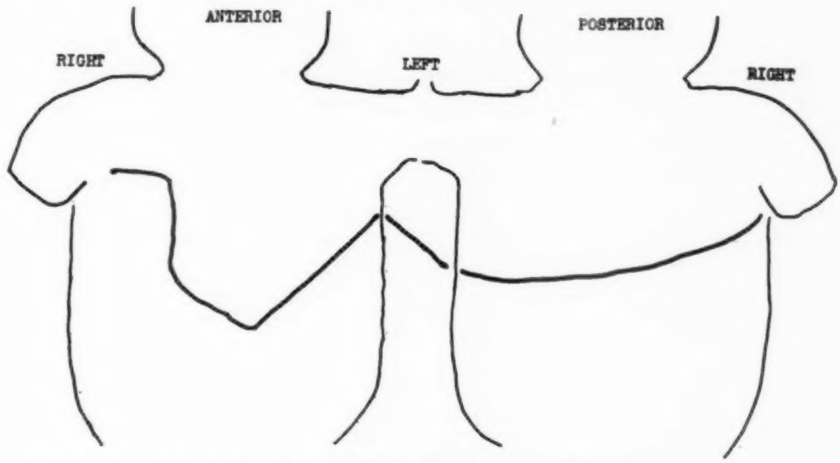

Fig. 2*A*.—Newborn girl, 6 hours old. Only the transitional zone is drawn in. The apparent irregularity in the diagram could be explained by direct reference to the living subject itself. It was seen that the angle at which the transitional plane intersected the chest wall and the noncylindrical shape of the latter could account for the seeming irregularity that appears in the two-dimensional diagram. The transitional plane is almost horizontal; the mean spatial QRS vector is almost vertical and points anteriorly.

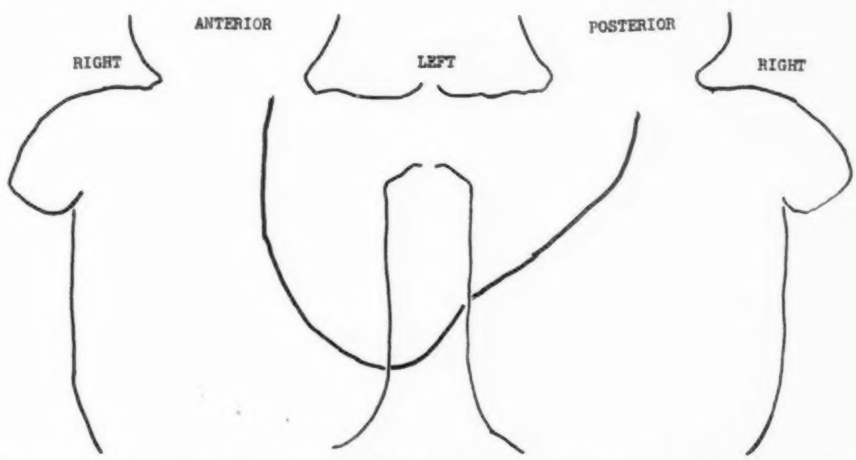

Fig. 2*B*.—Newborn boy, 3 hours old. Marked eccentricity of the transitional zone, its plane, and the center of the mean QRS vector. The transitional plane is almost vertical; the mean QRS spatial vector points almost horizontally to the right and somewhat anteriorly.

RESULTS

Figs. 1, 2*A*, and 2*B* illustrate how the chest was divided into positive and negative parts, separated by a transitional zone. Figs. 2*A* and 2*B* show the extreme variations found in the six cases. In the one infant examined five hours after birth and again three days later, there was no appreciable difference in the direction of the QRS vector or in the location of the transitional zone.

The form of the transitional zone is for the most part sharp and consistent with the intersection of a plane with the thoracic wall. Some parts show irregularities, but these are usually due to irregularities of the thoracic wall. If the myocardium adjacent to the electrodes supplied enough intrinsic potential to alter the QRS complex, then irregularities in the transitional zone ought to be seen in the precordial region where the heart is closest to the chest wall. This was not found and offers further evidence that the local effect of the myocardium adjacent to the electrode is not significant, even in the precordial leads of infants.

The transitional *zone* represents the intersection of the transitional *plane* with the chest wall. The plane passes perpendicularly through the center of the mean QRS spatial vector, and it corresponds to the zero-potential plane which bisects a dipole. All points on the plane are equidistant from the ends of the vector. Accordingly, a lead from anywhere on the plane or zone registers a transitional type of QRS complex.

Knowing the direction of the plane, one automatically knows the direction of the spatial QRS vector, for the latter is perpendicular to the former. Since the center of the vector is located somewhere on the plane, the location of the latter shows the possible locations of the center. The center of the vector corresponds to the center of ventricular activation. In the six cases studied the mean spatial QRS vector lay between 90 and 170 degrees in the frontal plane and it pointed slightly anteriorly in all cases. In four of the six cases the transitional zone defined planes which were located close to the left shoulder (Fig. 2*B*). This also locates the center of the mean QRS vector close to the left shoulder. Thereby a definite eccentricity of ventricular electrical activity is demonstrated. The eccentricity refers to the triangle whose apices are the shoulders and the pubis.

DISCUSSION

Part I. Eccentricity and Vector Analysis of the Neonatal Electrocardiogram.—The centers of the ventricular mass and the mean QRS vector should lie close to each other. The transitional zone should pass through or close to the center of the ventricular mass. In the newborn infant, on x-ray examination, the center of the ventricular mass lies relatively far to the left of the midline and near the left shoulder; accordingly, the center of the mean QRS spatial vector should also be close to the left shoulder. In Figs. 1 and 2*B*, the transitional plane passes to the left of the region which can reasonably be regarded as the center of the ventricular mass. This excessive eccentricity can be explained by the effect of eccentricity on the potential of the central terminal of Wilson. In this case the central terminal is dominated by the potentials of the left arm because the latter is closer to the heart than the other limb electrodes. The left arm is negative for the most part during the QRS phase in the newborn infant[1]; this makes the central terminal also negative during the QRS phase. This enlarges the area on the chest in which unipolar leads show positive QRS complexes as Ashman and associates[9] have suggested. Thereby the transitional zone is shifted even more to the left. One can expect any eccentricity that is demonstrated by the transitional zone method to be exaggerated beyond what is actually present.

Can the QRS complex in the newborn infant be analyzed in terms of the mean spatial vector? In adults, spatial vector analysis by Grant's method has been found reliable. In the newborn infant, however, its application encounters a serious obstacle in that the mean spatial vector shows a marked and unpredictable eccentricity.

The spatial vector is perpendicular to the axis of any transitional lead. Since this axis is a line drawn from the electrode of a transitional lead to the center of the vector, its construction is possible if the location of the center is known. In the adult it is assumed that the center of the heart and its vectors lie in a definite area, namely, the anatomical center of the heart, and deviations therefrom are clinically unimportant.[14] Consequently, it is possible to construct the axis of any transitional lead and derive the spatial vector from only one or two transitional chest leads in the adult.

In the newborn infant this method cannot be applied, for it is impossible to find the axis of one or two transitional *leads* because the center of the vector cannot be reliably assumed to lie in any given region. While it is possible to find the spatial vector from the transitional *zone*, the latter must be mapped out by multiple exploratory leads. This is impracticable. These statements are not intended to reflect adversely on the validity of spatial vector analysis of the electrocardiogram. Rather they merely indicate that the practical application of Grant's method is too difficult for clinical employment in the neonatal period.

Part II. The Effect of Eccentricity on the Correlation of the Vectorcardiogram With the Electrocardiogram.—Vectorcardiography, which promises to improve the diagnosis of neonatal right preponderance, is also affected by eccentricity of the heart. The practical application of the method is not seriously impaired by it because the placement of the electrodes in the cube system specifically attempts to correct for it. Eccentricity does make itself *felt* when the vectorcardiogram is compared to the routine electrocardiogram. The vector loops and the electrocardiographic complexes register the same electrical activity. From the vector loops it is theoretically possible to reconstruct the complexes of the various leads, and vice versa. Moreover, the general correlation between the two is good, although in the frontal plane certain discrepancies have been noted. We are inclined to believe that eccentricity of the heart, even in adults, is the cause of such discrepancies. Some reasons for this opinion may be cited.

Usually one translates the deflections in the limb leads into frontal heart vectors by orthogonal projection on the sides of an equilateral Einthoven triangle. It is assumed that the triangle is equilateral, that the heart is in its center, and that the conduction of the tissues is uniform. The fallacies of these assumptions were already appreciated by Einthoven; nevertheless, the ensuing errors, being of little importance, were disregarded. These fallacies intrude, however, when spatial vector analysis of the electrocardiogram is attempted in patients with marked eccentricity, as in the newborn infant. They interfere also in the adult when vector loops are correlated with the deflections in the limb leads. It then becomes necessary to take the eccentricity of the heart and the skewness of the triangle into account.

Burger and van Milaan[10] have devised a procedure for correcting the inaccuracies of the Einthoven triangle system. Experimentally they determined the effects of a given eccentricity on the limb leads. From this data they constructed a triangle on paper which permitted an accurate correlation between the deflections in the limb leads and the heart vector. After confirming this experimentally, Wilson and associates[11,12] elaborated the method so that it could be applied to the construction of a tetrahedral coordinate system for vectorcardiography. Although modern vectorcardiography seems destined to be based on the cube system of Duchosal and Sulzer, the theoretical considerations and findings of Burger and Wilson retain their practical significance.

They showed that the triangle which would correct for the eccentricity of the mean QRS vector in adults would have the approximate shape shown in Fig. 3,*A*. Note that *RL*, the axis of Lead I, forms an angle with the horizontal. If the direction of a given vector is known, then by simple inspection of this Burger triangle one can predict the type of deflection recorded in Lead I. This is accomplished by orthogonal projection of the vector on the axis of Lead I of the Burger triangle. The line *PC* is drawn from the center of the triangle perpendicular to *RL*, the axis of Lead I. All vectors pointing to the left (patient's left) of this perpendicular will project positively on the axis of Lead I and produce a positive deflection in that lead. Likewise, all vectors pointing to the right will give a negative deflection in Lead I. (The reverse process, the derivation of the heart vector from the deflections of the limb leads by means of the Burger triangle, does not concern us. It involves complex quantitative calculations, such as the division of the deflection by the length of the lead axis.)

Theoretically, Lead I has a horizontal axis, and it should record complexes identical in shape with those of any other horizontal lead. Because Lead I is not horizontal in an electrical sense, certain differences will appear between its deflections and those of a truly horizontal lead. Fig. 3,*B* shows the axis of Lead I, R_1L_1, taken from the Burger triangle in Fig. 3,*A*. Superimposed on it is R_aL_a, which is the axis of a truly horizontal lead, called Lead A. The respective perpendiculars are *wz* and *xy*. A vector located in the angle *wox* will inscribe a positive deflection in Lead I and a negative deflection in Lead A; likewise, a vector in the angle *yoz* will inscribe a negative deflection in Lead I and a positive deflection in Lead A. These may be called the angles of discrepancy.

Such discrepancies between Lead I and a horizontal lead have been recorded and published (though not recognized) by Grishman and his associates in a series of reports on vectorcardiography.[8,13] They employed a modification of the Duchosal and Sulzer cube system for the registration of the vector loops. One of its leads can be considered for our purposes truly horizontal; this is called Lead A. An inspection of the article by Scherlis and Grishman (Figs. 3, 7, 9, 14, and 16)[8] and the article by Lasser and Grishman (Figs. 6, 8, and 10)[13] shows distinct differences between Lead I and Lead A. The variations are in accord with the explanation in the preceding paragraph. This can be ascertained by noting in the accompanying frontal vector loops that the parts of the loops which correspond to the discrepancies lie in the angles described in Fig. 3,*B*.

This may suffice to demonstrate the practical soundness of the theoretical Burger triangle. The findings of Meyer and Herr[15] furnish additional experimental evidence that the axis of Lead I is tilted counterclockwise when the electrical source is located to the left of the center. For clinical use it is, of course, unnecessary to correct for the eccentricity of the heart in the interpretation of the electrocardiogram or vectorcardiogram. When the two methods are correlated with each other to test their mutual validity, then the correction of eccentricity is of value.

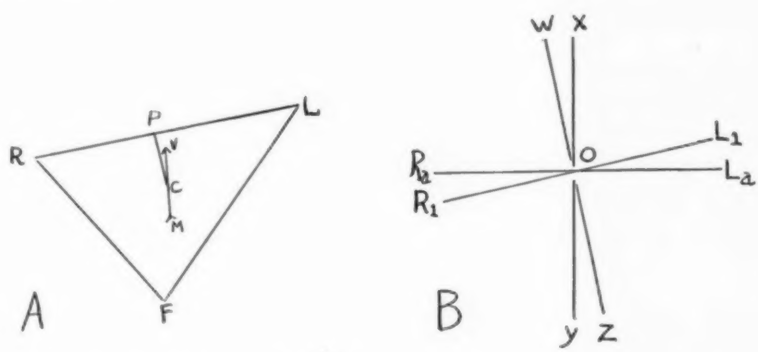

Fig. 3.—*A*, A triangle which, according to Burger, would correct for the eccentricity of the heart as found in the adult. *RLF*, the Burger triangle; *R*, right arm electrode; *L*, left arm electrode; *F*, left leg electrode; *C*, electrical and geometric center of the triangle; *RL*, the axis of Lead I; *CP*, perpendicular to *RL*; *MCV*, a heart vector which is vertical to the true horizontal and points upward. Note that *RL* forms an angle with the true horizontal and is rotated counterclockwise from it; note also that *MCB* projects positively on *RL*, so that a positive deflection is inscribed in Lead I.

B shows the location of those vectors which will inscribe a discrepant deflection in Leads I and A; the latter is the truly horizontal lead. R_1L_1, the axis of Lead I as it is electrically situated in the adult triangle; R_aL_a, the axis of Lead A. This is equivalent to the Lead A of the Grishman modification of the Duchosal-Sulzer cube system. *wz*, The perpendicular to Lead I; *xy*, the perpendicular to Lead A.

All vectors lying in the angle *wox* will project positively on Lead I and negatively on Lead A. All vectors lying in the angle *yoz* will project negatively on Lead I and positively on Lead A. All other vectors will give the same type of deflection in both leads.

SUMMARY AND CONCLUSIONS

The diagnosis of normal and abnormal right ventricular preponderance in the newborn infant needs to be improved. Grant's method of spatial vector analysis does not help because the marked eccentricity of the neonatal heart prevents its application. This eccentricity was demonstrated by mapping the transitional zone on the chest in six normal newborn infants. The center of the mean QRS spatial vector was shown to be close to the left shoulder. The effect of a given eccentricity on the central terminal and the resultant exaggeration of the eccentricity found by the transitional zone method is discussed.

Eccentricity is the cause of certain discrepancies between the electrocardiogram and the vectorcardiogram. Recourse was made to the triangle of Burger to explain such differences, some of which have appeared in the literature.

The authors thank Dr. Linn J. Boyd and Dr. David Scherf for their encouragement and advice in this work.

REFERENCES

1. Schaffer, A. I., Burstein, J., Mascia, A. V., Barenberg, P. L., and Stillman, N.: The Unipolar Electrocardiogram of the Newborn Infant, AM. HEART J. **39**:588, 1950.
2. Schaffer, A. I.: Unipolar Electrocardiographic Studies in Congenital Heart Disease in Infancy, Am. J. Dis. Child. **80**:260, 1950.
3. Alimurung, M. M., Joseph, G. L., Nadas, A. S., and Massell, B. F.: The Unipolar Precordial and Extremity Electrocardiogram in Normal Infants and Children, Circulation **4**:420, 1951.
4. Ziegler, R. F.: Characteristics of the Unipolar Precordial Electrocardiogram in Normal Infants, Circulation **3**:438, 1951.
5. Grant, R. P.: Spatial Vector Electrocardiography. A Method for Calculating the Spatial Electrical Vectors of the Heart From Conventional Leads, Circulation **2**:676, 1950.
6. Scherlis, L., Lasser, R. P., and Grishman, A.: Spatial Vectorcardiography: The Normal Vectorcardiogram. VI, AM. HEART J. **42**:235, 1951.
7. Lasser, R. P., Borun, E. R., and Grishman, A.: Spatial Vectorcardiography: Right Ventricular Hypertrophy. VII, AM. HEART J. **42**:370, 1951.
8. Scherlis, L., and Grishman, A.: Spatial Vectorcardiography: Myocardial Infarction. V, AM. HEART J. **42**:24, 1951.
9. Ashman, R., Ferguson, F. P., Gremellion, A. I., and Byer, E.: The Normal Human Ventricular Gradient, AM. HEART J. **29**:697, 1945.
10. Burger, H. C., and van Milaan, J. B.: (a) Heart Vector and Leads, Brit. Heart J., **8**:157, 1946; (b) Heart Vector and Leads, Part II, Brit. Heart J. **9**:154, 1947.
11. Wilson, F. N., Bryant, M., and Johnston, F. D.: On the Possibility of Constructing an Einthoven Triangle for a Given Subject, AM. HEART J. **37**:493, 1949.
12. Wilson, F. N., and Bayley, R. H.: The Electrical Field of an Eccentric Dipole in a Homogeneous Spherical Medium, Circulation **1**:84, 1950.
13. Lasser, R. P., and Grishman, A.: Spatial Vectorcardiography: Right Bundle Branch Block. VIII, AM. HEART J. **42**:513, 1951.
14. Grant, R. P.: The Relationship of Unipolar Chest Leads to the Electrical Field of the Heart, Circulation **1**:878, 1950.
15. Meyer, P., and Herr, R.: The Electrical Axis of an Artificial Dipole Obtained by Means of Standard and Thoracic Leads, Arch. d. mal. du coeur **41**:325, 1948. (Abstracted in AM. HEART J. **38**:632, 1949.)

THE ROLE OF A SOCIAL AGENCY IN A REHABILITATION PROGRAM FOR THE CARDIAC PATIENT

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NEW YORK, N. Y.

ALL services and facilities, medical, psychological, social, and economic—from diagnosis to placement—affect the "re-enablement" of the patient.

Dr. Alan Gregg of the Rockefeller Foundation cautioned us that in our experiment in the rehabilitation of the cardiac patient (started in February, 1948) Altro would relive many of the experiences of more than three decades ago. In many respects the concepts and attitudes toward heart disease parallel those toward tuberculosis in 1913 when our agency was organized.

We found many comparable areas. The medical profession was concerned with diagnosis and treatment almost to the exclusion of the patient as an individual, a worker, a member of a family and the community. There was much contradictory advice and little in the way of objective tests of work capacity or potentials. Because of fear of exacerbation of the disease, many doctors and families were discouraging the idea of work for the patient. A patient, who had been told that he could work, found resistance on the part of employers.

The reasons for refusing employment often related to financial liability. The insurance company was said to object. The excessive risk would result in penalties due to bad experience. It was felt these patients would make undue demands on employer-paid life insurance or retirement plans.

Many years ago, concerned with this same attitude toward employment of the tuberculous patient, three of the largest carriers of accident insurance were contacted.†

One replied, "As far as I know, no insurance company has expressed any attitude either for or against employment of arrested cases of tuberculosis. This company has been re-employing tuberculous workers over a period of twenty years." Another said, "It is safe from a medical viewpoint and philanthropically

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Recently we had the opportunity of hearing Mr. Hochhauser give an address in which he outlined the experiences of the Altro Health and Rehabilitation Services with the arrested case of tuberculosis. In the course of his remarks, he made reference to Altro's extension of their clientele to include a group of cardiac patients. This was, in a way, an exploratory venture or an experiment. We were deeply interested, and expressed the hope that he might, at an early date, let our readers know how the project had developed over its first three years, and he generously consented to do so. We are grateful to him for a brief account of this experiment, the philosophy and progress of which may well be a milestone in the solution of an ever-increasing medical, social, and economic problem.

Editor

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†Hochhauser, E.: Industrial Aspects of the Rehabilitation of the Tuberculous. Transactions of the 34th annual meeting of the N.T.A., 1938.

wise." Only recently J. Dewey Dorsett, General Manager, Association of Casualty and Surety Companies, wrote in "Performance" of "the outworn myth that insurance companies forbid the employment of the physically handicapped." The difficulty in securing employment for cardiac patients is aggravated by employers' unwillingness to engage men and women over 40 years of age. With heart disease, as with tuberculosis, unemployment is not only an economic problem, but in indolence we have the psychological and social factors that often result in recurrent or prolonged illness. Financial assistance during convalescence and rehabilitation is often essential, but pensions, under any name, and no matter how they may be safeguarded, are no substitute for an opportunity to work. Pensions that are not part of a scheme of rehabilitation tend to make rehabilitation impossible and permanent pensions inevitable.

In England the Ministry of Labour through its "Remploy Limited" owns and operates some sixty sheltered workshops for the disabled, including the cardiac and tuberculous patients. These shops can serve from fifty to 300 persons. Their plans call for 140 such workshops by 1954. Private agencies operating sheltered workshops receive two-thirds of their deficits in operation up to 80 pounds sterling per person.

Apparent indifference on the part of industry gives credence to the claim of the handicapped that only under compulsion can they expect employment. Returning to a job after successful treatment, or to a readjusted job with a former employer, has many advantages for the patient. It pays both, as truly as in neglect they both pay.

Public agencies have accepted the responsibility for vocational training and placement where indicated. Private agencies can and often do play an important part in assisting the public agencies: referring clients, supplementing and interpreting public services, and in influencing state and Federal appropriations for these services.

Vocational guidance, retraining for a more suitable or remunerative job, will meet the needs of many clients. For some there is need for an intermediary service between illness and vocational guidance or a job. Twenty-five years ago Dr. Hubert Guile, then Chief of the Cardiac Service at Bellevue Hospital, urged that we accept cardiac patients at our Altro Work Shops. Our scheme of graduated work activity, with medical and social care and economic assistance for the patient and his family, would enable many cardiac patients, prematurely condemned to the scrap heap, to enjoy years of useful, productive living. Cardiac patients, Dr. Guile told us, present many of the physical and psychological problems common to the tuberculous patient. The patient's fear is as great a hazard as his physical limitations, and there are many unwarranted prejudices on the part of the patient and his family, as well as the employer, that are common to the tuberculous patient.

One of the deterrents in starting the cardiac project was the fear of fatal episodes while at work, and the effect of such an experience on our tuberculous patients. Cardiologists whom we consulted stated that the careful medical observation provided at Altro would enable us to detect those who were "going

bad" and secure medical treatment for them. They also assured us that very few deaths occur while at work or could be attributable to a graduated work program.

The Federation of Jewish Philanthropies, before making the financial grant we requested, consulted a small group of specialists in cardiovascular diseases and in tuberculosis, together with some prominent laymen. Cardiologists who knew of Altro's services had approved of such an experiment.

Instead of being overwhelmed with suitable applicants, it took more than two years before we reached the quota of twenty. Later, this was raised to twenty-five, and in August of 1950, when that number was reached, our quota was raised to thirty.

Of the seventy-seven cardiac patients who have been at Altro Work Shops since February, 1948, not one has expressed any fear of tuberculosis. Because of the often indiscriminate fear, and also as an added protection to the patient, admission was limited to cardiac patients found free of clinical tuberculosis, but who has been previously exposed as shown by a positive tuberculin test. Within the age group accepted we found practically all of the applicants had a positive skin reaction. Our only exception, a 19-year-old boy with rheumatic heart was terribly disappointed when told that his negative reaction made him ineligible. We explained that a BCG inoculation usually results in a positive reaction within six weeks. The patient consulted his doctor, who secured the mother's approval, and six weeks after the inoculation with BCG he had a positive reaction. He was admitted to Altro and has done exceedingly well.

Patients between the ages of 18 and 55, physically and/or psychologically not ready for work or vocational training, were considered for admission. They were accepted if in the opinion of our cardiologist they might, after a reasonable time at the workshop, be prepared for placement in carefully selected jobs, for self-employment, or vocational training. Those able to work a full day but unable to find a job, or in need of vocational training, were not eligible.

We admitted patients in classifications II C,D to III C,D, including thirty with hypertensive arteriosclerotic heart disease, and twelve with rheumatic or congenital heart disease. In our second and third year six patients with auricular fibrillation were admitted. The prognosis in the latter group was guarded. One died and the other five continue to work but appear to require permanent sheltered employment. We had not planned to admit long-term cases during the experimental period, although it was our hope that our facilities might be expanded to include a limited number of such patients.

The sixth cardiac patient admitted to Altro, a veteran of World War II, was classified as IIIC arteriosclerotic heart disease. His first episode was while in the Navy, and the second, ten months before admission. The doctor at the Veterans Administration Hospital persuaded him to visit Altro, but it took several sessions with the social worker to convince the patient, who was taking digitalis daily, that he might start on a limited work schedule. The transformation in this patient's attitude within a few months prompted one of the doctors at the Veterans Administration to say that a miracle had occurred. Our doctor's report states "the findings on examination for admission to Altro showed no ob-

jective evidence of heart failure. There was expressed intense fear of the likely bad cardiac effect that might follow work. After having worked for a short time the entire psychic picture changed. Less irritability and greater willingness to work without fear of a heart attack was noticed. Work hours were gradually increased until six hours were allowed each day. During the course of employment no objective signs of heart failure were found. Though the complaints made were later considered to be unrelated to heart disease, such a conclusion could not have been drawn without this long period of observation. After self-assurance had been gained, work capacity developed faster. On discharge the minor subjective complaints which previously had caused disability were no longer prevalent, and the ability to work was unquestioned."

The patient's comments at the time of graduation are also significant. "I did not work because the doctor told me not to work. So I came to Altro and got back a lot of self-confidence, maybe because I knew we had a nurse and a doctor there; but later, after I had been there a while, I found that supervision was no longer essential, and I did not want to continue on it. I regained my self-confidence knowing that I was able to do something and have the ability to go back to work. I wouldn't have been able to do eight hours' work before."

Patients are referred by private and public agencies, medical clinics, and private physicians. Those requiring medical treatment continue to receive such treatment from the clinic, private physician, or hospital referring them.

As with the tuberculous patient, the work period is divided so that the patient on a four-hour work schedule works two hours in the morning and two hours in the afternoon. Rest periods are taken either in the roomy and airy indoor lounges or on the roof garden. There is a short respite in the midmorning and afternoon and those who want milk get it in the cafeteria without charge. Luncheons are served at cost. As work hours increase, rest periods decrease until the patient is working normal hours.

Cardiac patients are examined by the staff cardiologist once a week at the workshop. Electrocardiograms are taken weekly during the first month and then as ordered by the cardiologist. The shop nurse keeps a record of subjective complaints as well as pulse rates at various times during the day. A social worker interviews the patients at the workshop once a week. Patients of all creeds and color are accepted. They come from skilled and unskilled trades, white collar jobs, the professions, and, with our young rheumatics, with no background of work experience.

Altro makes and sells washable service apparel to hospitals and industry. Patients usually start at the sewing machine, a sedentary job approved for cardiac as well as tuberculous patients. We had one cardiac patient, formerly a cutter in the garment industry, who subsequently was transferred to the cutting table and later graduated to industry. If a patient wishes to become a skilled garment worker he receives more intensive instruction than if the purpose is solely physical and psychological rehabilitation. After graduation the patients return to school, to their old jobs if suitable, are placed in a new job, or, through the State Division of Vocational Rehabilitation, are given vocational training.

Patients are paid at a piece rate never less than that paid for comparable work in industry. The output is sold competitively at a price not less than that charged by industry. When necessary, earnings and/or public assistance are subsidized by the Altro Health and Rehabilitation Services, Inc. so that the patient and his family are assured the necessary minimum for their requirements. Our approach to rehabilitation is on a family basis rather than on an individual patient basis. The medical, social, and, where necessary, psychiatric or economic care of the patient and his family are essential services. We know that to treat the patient and neglect the family is as unsound medically as it is socially. The Federation of Jewish Philanthropies provides most of the funds required for medical and psychiatric care, as well as for the subsidy. The Greater New York Fund assisted for two years.

The primary limitation of patients referred thus far was their fear of engaging in any activity. This becomes a major psychological disability.* The expressed fear that exertion may result in deterioration of the cardiac condition may, in part, be traced to the oversolicitousness of the medical advisors. Newspapers and radio, by overemphasizing and overpublicizing the acute accidental deaths, add to the havoc.

Though the group observed is small in number, the observations indicate that ordinary occupation which does not entail more than usual exertion may not be detrimental to the health of the cardiac patient. On the contrary, relief from anxiety and return to a normal working existence, including resumption of normal social relationships and economic independence, may be of benefit to the course of heart disease.†

Three decades ago tuberculous patients, on discharge from sanatoriums, were given a long list of "don'ts," but little or nothing in the way of "do's." Fearful lest their disease become reactivated, confused with contradictory advice by physicians, rejected by friends, employers, and sometimes family, the percentage of readjusted patients was low.

The cardiac patient today is having many of the same experiences. As our cardiologist put it, "The difficulty of the cardiac to find employment is paralleled by his fear to accept a job when one is available. The years of invalidism, the possible recurrence of a heart seizure, and the oft-repeated advice to avoid exertion, are a constant source of anxiety and economic insecurity. There is no general agreement as to the ability of the cardiac to work. Following a seizure of myocardial infarction, the cardiac is impressed with the 'don'ts,' and he gets little information of what he can do."

There is a calculated risk in serving the cardiac patient. In our limited experience there have been deaths, not always with apparent explanation, such as the widower who played baseball with his two sons and walked home after the game, and the patient whose wife, after a quarrel, hit him over the head with a bottle. There were four deaths, none at the workshop.

As with the tuberculous patient we know of no practical objective test of work capacity. After a long stay in the protective atmosphere of a hospital, the

*Haselkorn, Florence, and Bellak, Leopold: "A Multiple-Service Approach to Cardiac Patients."
†From a report by Dr. Abraham Jezer on two years' experience in cardiac rehabilitation.

psychological as well as the physical demands that come with living again in the home and in the community, traveling to and from the workshop or job, must be considered as well as the physical demands of work. Marital discord often is more devastating than work itself. At Altro all the factors receive consideration and are evaluated in setting the hours of employment. The careful medical supervision by qualified physician and nurse are all of inestimable value, but even more important is the observation in the work environment provided at Altro.

The whole physical setup and the operative procedures impress the patient and influence those with overwhelming fears, so that they are willing to try it out. The New York Heart Association, in its Quarterly (November, 1949), captioned its article on our service "Altro, a Clinic in Confidence." Our cardiac experiment up to date cannot give us a statistical base for conclusions. It is hoped that it may give us some objective test for determining work capacity that is not based on laboratory tests nor isolated from everyday living. It has helped a number of men and women to productive, useful living, probably to longer and more satisfying lives. It definitely serves the community by reducing the cost of the patients' medical care and financial assistance. Although most of the graduates have found employment, the cardiac patient appears to have even more difficulty than the tuberculous patient in securing work.

Two physicians associated with large industries assured us that their companies' policies were typical of those with good employment practices. An employee with heart disease may return on a part-time basis, but no new applicant with any form of heart disease will be accepted for employment. As one physician said, "I know that work is often essential if the patient is to stay well, but it is not considered good business to take on a worker with heart disease."

What is the risk in employing the cardiac patient? If there is a risk, who should bear it—the employer, the insurance company, the community, or the patient? The community, in a very real sense, bears the cost financially and socially if a patient who can work is not permitted to work. The employer, as a large taxpayer, is not relieved when he denies any responsibility. A discussion of all concerned—with public health and social security represented—might find some suitable way of sharing any risk. The returns would be great.

Clinical Reports

VENTRICULAR TACHYCARDIA FOLLOWING PROCAINE AMIDE HYDROCHLORIDE (PRONESTYL) AND QUINIDINE

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IT HAS long been known[1,2,3] that quinidine sulfate exerts, as two of its many pharmacologic actions, peripheral blocking of vagal activity, (atropine-like) and depression of electrical conduction within the myocardium. This action is most marked in the ventricles and frequently produces intraventricular or bundle branch block. Indeed, widening of the QRS complex has long been used as a clinical guidepost in quinidine therapy.

The popular use of quinidine to depress auricular conduction and convert auricular fibrillation to regular sinus rhythm has led to the clinical impression that aberrant ventricular rhythms due to quinidine are for some reason more common in hearts with pre-existing auricular fibrillation. Wilson and associates[4] have made the statement that aberrant rhythms occur in one-third to one-half of such cases. Scattered reports have appeared in the literature and we have attempted to summarize them in Table I.

TABLE I. QUINIDINE THERAPY OF AURICULAR FIBRILLATION. INCIDENCE OF ABERRANT VENTRICULAR RHYTHM

AUTHOR	CASES TREATED	ABERRANT VENTRICULAR RHYTHMS
Levy[6]	11	3
Maynard[16]	53	1
Korns[2]	35	1
White et al.[9,15]	75*	6
Jezer and Schwartz[8]	1†	1
Wilson et al.[4]	?	2
Gouaux and Ashman[10]	1	1

*Including 4 cases auricular flutter.
†Auricular flutter.

Two series have been collected by the authors. All cases with auricular fibrillation, in which conversion with quinidine was attempted, were collected

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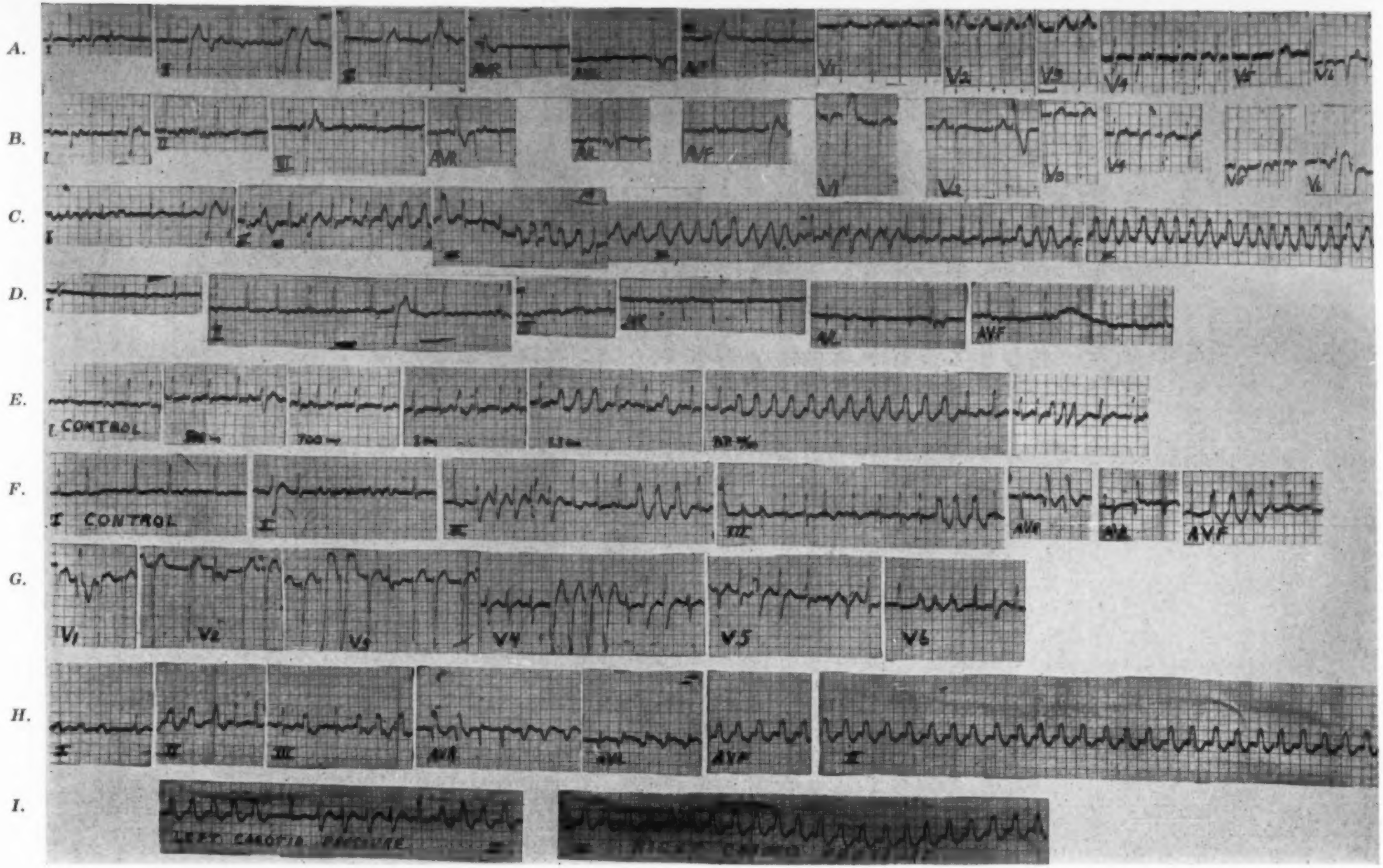

Fig. 1.—*A*, (10-10-50) Weight 216. In frank congestive failure with râles and edema. Off digitalis and all medication for one month. Venticular rate, 140. Venticular premature contractions from at least two foci. *B*, (10-18-50) Weight 197. Out of frank failure. No medication. Ventricular rate, 130. *C*, (10-19-50) Standard leads and strip of Lead II taken during intravenous administration of Pronestyl. 800 mg. has been injected. Runs of ventricular premature contractions from two foci? Blood pressure fell to 80/60 mm. Hg during end of injection but rose again while still in the aberrant rhythm. *D*, (10-19-50) One hour later after intravenous digoxin 1.0 mg. *E*, (10-20-50) Intravenous Pronestyl after complete digitalization, completed dose indicated on each strip. Aberrant rhythm did not become well established until after 1100 mg. of Pronestyl. *F*, (10-23-50) After 2.0 Gm. quinidine by mouth in 7 hours. *G*, (10-23-50) Precordial leads after 2.0 Gm. quinidine. *H*, (10-24-50) After 3.0 Gm. quinidine in 10 hours. *I*, No effect from carotid pressure.

from the Mt. Alto Veterans Administration Hospital records over a two-year period. Of the twenty-one cases of young and middle-aged patients, seven instances of aberrant ventricular rhythm were discovered. Another series of cases of forty-four elderly patients was collected from the Soldiers' Home.* This was a consecutive group with auricular fibrillation in whom conversion was attempted with quinidine and strychnine. In the forty-four cases, there were two instances of frequent extrasystoles and three of aberrant ventricular rhythm. These data are summarized in Table II. Thus the incidence of aberrant rhythm in treated auricular fibrillation is variable but appreciable.

The complex pharmacologic properties of quinidine have made it almost impossible to define the mechanisms involved. These rhythms have been called ventricular in origin by Cohn and Levy,[5] Levy,[6] Lewis and associates,[1] Schwartz and Jezer,[7,8] and others; they have been called instances of defective intraventricular conduction with supraventricular origin of the impulse by Wilson and associates,[4] White and associates,[9] Gouaux and Ashman,[10] and Barker and associates.[11]

TABLE II. AURICULAR FIBRILLATION TREATED WITH QUINIDINE

SERIES	CASES	ABERRANT VENTRICULAR RHYTHMS	FREQUENT EXTRASYSTOLES
Mt. Alto	21	7	1
Soldiers' Home	44	3	2

Recent pharmacologic data presented by Dutta[12] points to at least one common site of action of different types of compounds in common use. Atropine, pethidine, procaine, and quinidine were all found by this author to possess a ganglionic blocking action in the superior cervical ganglion. Intravenous procaine has been known occasionally to produce premature ventricular complexes singly and in runs, both clinically (Schaffer and associates[13]) and in animals (Uhley and associates[14]).

With these pharmacologic and experimental relationships, it would not be surprising to find that the recently introduced procaine derivative, Pronestyl, occasionally produces some of the aberrant rhythms already described for procaine and quinidine.

A case is presented in which under controlled observation an aberrant ventricular rhythm was produced after (1) intravenous Pronestyl without digitalization, (2) intravenous Pronestyl after digitalization and (3) oral quinidine on two occasions. Details of therapy are described in the legend of Fig. 1.

The case is presented in detail because it illustrates a cardiac effect common to both Pronestyl and quinidine and is the first known report of such toxicity clearly attributable to Pronestyl. Since the patient had pre-existing auricular fibrillation, the report recalls earlier controversy concerning the interpretation of these aberrant ventricular rhythms.

*Courtesy of Dr. Lee Miller.

CASE REPORT

History.—A 31-year-old Negro man complained of chest pain and shortness of breath progressing over six months.

At the age of 22, he had a Type I pneumococcus pneumonia with septicemia. He had twelve days of high fever while being treated with gluco-sulfapyridine. Electrocardiograms at that time showed sinus tachycardia. Debility continued for six weeks after discharge. Later he had brief episodes of knee and shoulder pain, sweating, and flushed sensation. Eight months before admission he developed dyspnea. Electrocardiograms showed auricular fibrillation. He developed increased dyspnea, orthopnea, severe cough, and occasional sharp precordial pain. There was a history of gonorrhea and syphilis with positive serology after five courses of therapy.

Physical Data.—The patient had rapid, labored breathing, and an irregular pulse of 120; the blood pressure was 140/100 mm. Hg. The jugular veins were distended. There were musical expiratory wheezes throughout, with fine, moist râles at both lung bases. The apex beat was in the fifth intercostal space at the anterior axillary line, and was grossly irregular. The pulmonic second sound was loud and split, and the mitral first sound was variable. No murmurs were audible. Marked leg varicosities with incompetent communicating veins were noted.

Laboratory Data.—The heart was enlarged in the x-ray picture. The transverse diameter was 19.3 cm. (25 per cent above "normal"). The barium-filled esophagus was displaced posteriorly and the right ventricle was prominent in the oblique view. The impression was enlargement of all chambers rather than a mitral configuration. Lung markings were increased.

Electrocardiograms showed auricular fibrillation with frequent extrasystoles similar to the control tracing in Fig. 1.

The venous pressure was 220 mm. of saline. The circulation time was arm to lung, 20 seconds, arm to tongue, 25 seconds. The vital capacity was 2.6 liters (55 per cent of normal).

Hospital Course.—The patient was given intravenous Pronestyl as detailed in the legend of Fig. 1. The succeeding events are shown in the illustration. He had two episodes of numbness and pain in the chest and left arm with ulnar radiation. On the seventeenth hospital day he developed suddenly and successively ocular pain, partial blindness, slurred speech, numbness of left side, left facial paralysis, paralysis of left arm and hand, hyperhidrosis, and weakness of left leg. He was treated immediately with anticoagulants with complete clearing of the neurological findings. He progressively improved and returned to work with his employer's cooperation in restricting his activity.

Diagnosis.—1. Heart disease of unknown etiology; enlarged right and left ventricle; congestive heart failure; auricular fibrillation with frequent ventricular extrasystoles. 2. Cerebral embolus. 3. Possible pulmonary embolus. 4. Syphilis, treated but with persistent positive serology. 5. Varicose veins.

DISCUSSION

This case presents many problems. First, is this aberrant rhythm an unequivocal Pronestyl effect? The progressive lengthening of the runs of aberrant complexes during mounting intravenous dosage would suggest this, as the aberrant rhythm became established after 800 mg. of Pronestyl, (given in 100 mg. fractions). Since the form of the complexes in the early runs resembles the pre-existing ventricular premature contractions from more than one focus, it seems likely that these foci were the source. Once established, the aberrant rhythm continued uninterrupted for more than five minutes until intravenous digoxin was given, after which it reverted to the previous pattern. This normal pattern was recorded intermittently for ninety minutes. The ventricular rate was 100 and infrequent ventricular premature systoles were seen. Repetition of the phenom-

enon the following day after complete digitalization and its recurrence on two subsequent occasions under quinidine therapy would strongly suggest a cause and effect relationship.

It might be suggested that this was a sensitivity phenomenon. The lack of previous exposure to these agents, the negative skin tests to procaine and Pronestyl, and the similar effects noted with quinidine make drug sensitivity an unlikely explanation.

It has been indicated in the literature that many cardiac therapeutic agents have paradoxical effects under specific conditions. Depressant drugs may produce or aggravate irritable phenomena. Pronestyl has been advocated as a successor to quinidine in many arrhythmias. The only toxic reaction emphasized has been its ganglionic blocking effect producing hypotension if given rapidly and its tendency to produce sensitivity if given over a long time.

It seems likely that with increasing clinical experience, paradoxical effects like those illustrated will be noted more frequently. If the experience with quinidine as presented in Tables I and II is a valid analogy, caution should be greatest in the presence of auricular fibrillation.

SUMMARY

1. Treatment of auricular fibrillation with quinidine raises the problem of aberrant ventricular rhythms which occur with appreciable frequency.

2. The pharmacologic similarities of procaine, quinidine, and atropine are noted.

3. A case is described in which ventricular tachycardia followed on two occasions the administration of Pronestyl or of quinidine.

4. This is the first known report of ventricular tachycardia following Pronestyl.

REFERENCES

1. (a) Lewis, T., Drury, A. N., Iliescu, C. C., and Wedd, A. M.: Observations Relating to the Action of Quinidine Upon the Dog's Heart; With Special Reference to Its Action on Clinical Fibrillation of the Auricles, Heart **9**:55, 1921.
   (b) Lewis, T., Drury, A. N., Wedd, A. M., and Iliescu, C. C.: Observations Upon the Action of Certain Drugs Upon Fibrillation of the Auricles, Heart **9**:207, 1922.
2. (a) Korns, H. M.: An Experimental and Clinical Study of Quinidine Sulphate: Experimental: Arch. Int. Med. **31**:15-35, 1923; Clinical: Arch. Int. Med. **31**:36, 1923.
   (b) Korns, H. M.: Delayed Conduction Through Right and Left Branches of Atrioventricular Bundle, Arch. Int. Med. **30**:158, 1922.
3. Gold, H., Otto, H. L., and Satchwell, H.: The Use of Quinidine in Ambulatory Patients for the Prevention of Paroxysms of Auricular Flutter and Fibrillation; With Especial Reference to Dosage and the Effects on Intraventricular Conduction, AM. HEART J. **9**:219, 1933.
4. Wilson, F. N., Wishart, S. W., Clark, N. F., and Herrmann, G. R.: Nature of Abnormal Ventricular Complexes During Quinidine Treatment of Auricular Fibrillation, Proc. Soc. Exper. Biol. & Med. **23**:273, 1926.
5. Cohn, A. E., and Levy, R. L.: Experimental Studies of the Pharmacology of Quinidine, Proc. Soc. Exper. Biol. & Med. **18**:283, 1921.
6. Levy, R. L.: Clinical Studies of Quinidine, Arch. Int. Med. **30**:451, 1922.
7. Schwartz, S. P., and Jezer, A.: Actions of Quinidine and Quinine on Patients With Transient Ventricular Fibrillation, AM. HEART J. **9**:792, 1934.
8. Jezer, A., and Schwartz, S. P.: Unusual Manifestations Following the Use of Quinidine Sulphate in a Patient With Auricular Flutter, AM. HEART J. **10**:124, 1934.

9. White, P. D., Marvin, H. M., and Burwell, C. S.: The Action of Quinidine Sulphate in Heart Disease, To Abolish the Circus Movement of Auricular Flutter and Fibrillation, Boston M. & S. J. **185**:647, 1921.

10. Gouaux, J. L., and Ashman, R.: Auricular Fibrillation With Aberration Simulating Ventricular Paroxysmal Tachycardia, Am. Heart J. **34**:366, 1947.

11. Barker, P. S., Johnston, F. D., and Wilson, F. N.: The Effect of Quinidine Upon Sinus Tachycardia Including the Production of Transient Bundle Branch Block, Am. Heart J. **25**:760, 1943.

12. Dutta, N. K.: Pharmacologic Properties Common to Atropine, Pethidine, Procaine, and Quinidine, Brit J. Pharmacol. **4**:197, 1949.

13. Schaffer, A. I., Steinman, R., and Scheaf, D.: Intravenous Procaine: Its Effect on the Human Electrocardiogram and on Cardiac Arrhythmias, Cardiologia **16**:342, 1950.

14. Uhley, M. H., and Wilburne, M.: Effect of Intravenous Procaine on Electrocardiogram of Dog, Am. Heart J. **36**:576, 1948.

15. Viko, L. E., Marvin, H. M., and White, P. D.: A Clinical Report on the Use of Quinidine Sulfate, Arch. Int. Med. **31**:345, 1923.

16. Maynard, E. P.: Five Years' Experience in the Treatment of Chronic Auricular Fibrillation With Quinidine Sulphate, Am. J. M. Sc. **175**:55, 1928.

NODAL TACHYCARDIA IN A CASE OF ROCKY MOUNTAIN SPOTTED FEVER

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Rocky Mountain spotted fever is not a common disease, and despite its name it may occur in any part of the United States. When it occurs in an endemic area, it is more easily recognized than the occasional sporadic case. In the latter instance, the disease should be suspected when a patient complains of headache, prostration, chills, fever, and bone pain and when a maculopapular rash appears on the extremities. When these symptoms appear and there is a history of tick bite, the diagnosis can usually be confirmed by agglutinations with Proteus OX19 in a titer of 1:320 or over, and/or complement fixation test in a titer of 1:10 or over, or animal inoculation.

In the untreated cases, the fatality rate is 20 to 25 per cent. Since the advent of the new antibiotics Chloromycetin and aureomycin, the disease can now be successfully treated. Pincoffs and associates[1] have reported seventeen cases of Rocky Mountain spotted fever successfully treated with Chloromycetin. Parker and co-workers[5] have also reported on the efficacy of Chloromycetin as a chemotherapeutic agent in sixteen cases of Rocky Mountain spotted fever. Ross and associates,[2] Cooke,[3] and Havens and Stickney[4] have reported cases in which the disease was successfully treated with aureomycin.

It is the purpose of this article to report a patient with Rocky Mountain spotted fever who made an excellent clinical response to Chloromycetin, but in whom an intermittent nodal tachycardia was discovered during the course of the disease which persisted after clinical recovery.

CASE REPORT

D. B., a 21-year-old white man, was admitted to this hospital on July 31, 1951. He had been perfectly well until July 28, at which time he noted headache, dizziness, chills and fever, slight cough, and a mild rash on the extremities. Five days earlier (July 23), while on maneuvers at Fort Dix, N. J., he was bitten by a tick in the region of the left nipple. In removing the tick, which had become adherent to the skin, he caused the slight extrusion of a few drops of blood.

Physical examination on admission revealed an acutely ill white man with flushed facies. The temperature was 103.2° F. orally, the pulse 120, the blood pressure 120/80 mm. Hg. The patient was prostrated. There was a faint macular rash on the arms, forearms, and legs and a

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maculopapular rash on the chest and back. At the region of the left nipple there was a small scar, caused by the extrusion of the adherent tick. The lungs were clear and resonant. Examination of the heart revealed a grossly irregular rapid rhythm, accompanied by a soft systolic murmur. The remainder of the physical examination, including neurological examination, was negative.

Laboratory Work.—The red blood cell count was 4.6 million; the hemoglobin, 13.2 Gm.; sedimentation rate, 11; hematocrit, 44; the white blood count, 7,100 with a differential consisting of 16 per cent bands, 52 per cent segmented cells, and 32 per cent lymphocytes. Agglutinations for typhoid, paratyphoid, and undulant fever were negative. A cold agglutination test was negative; a heterophil antibody test was negative. On July 31 agglutinations for Proteus OX19 were negative; on August 9 they were 1:86 and on August 14 1:320. Spinal fluid examination, blood cultures, and urinalysis were negative. Blood smears for malarial parasites were negative. A roentgenogram of the chest on July 30 was negative. An electrocardiogram on the same day revealed a sinus rhythm with dominant intermittent nodal tachycardia (Fig. 1). There were no ST or T-wave changes indicative of myocardial damage.

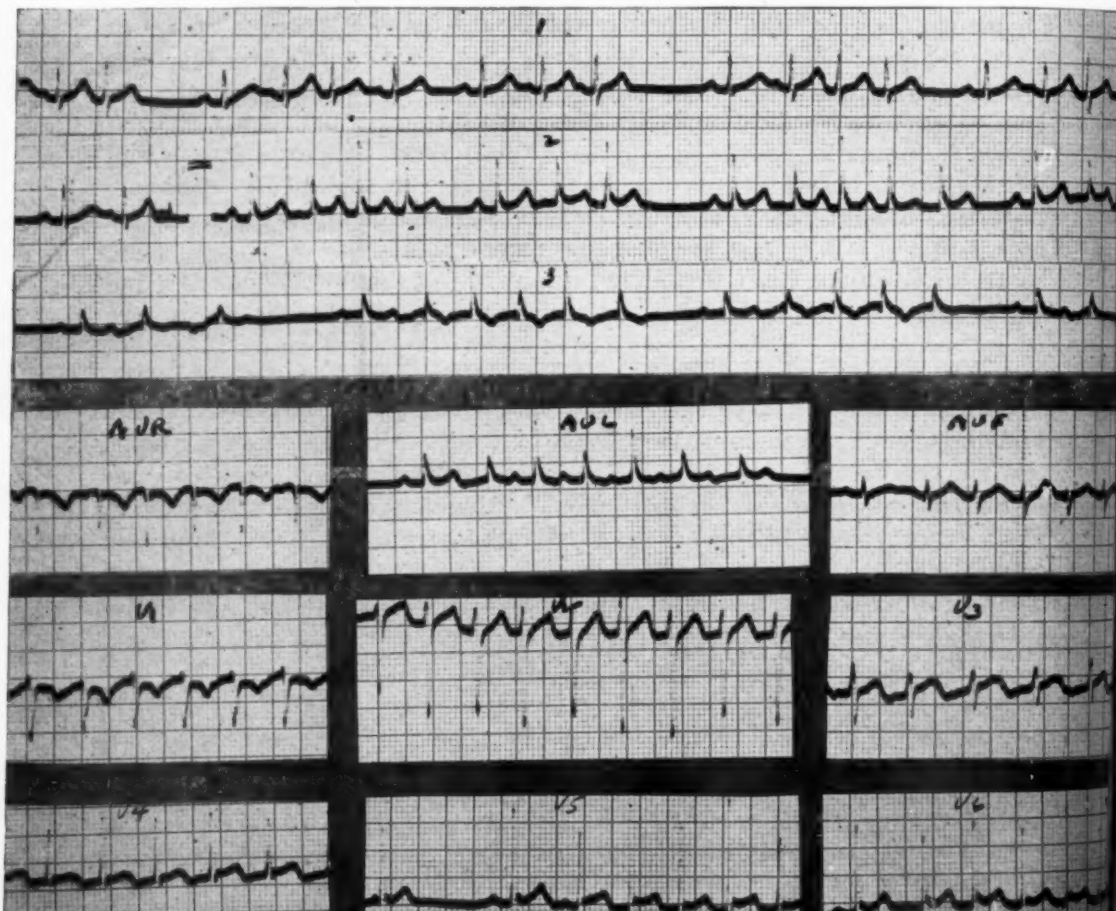

Fig. 1.—This tracing, taken during the course of the disease, shows a sinus rhythm with intermittent nodal tachycardia. The tracing is normal except for the rhythm.

Course in the Hospital.—The diagnosis of Rocky Mountain spotted fever was suspected soon after the patient was admitted, and on August 1 he was started on Chloromycetin. He was given

1 Gm. initially and 500 mg. every six hours for one week. Within twenty-four hours after initiation of Chloromycetin therapy there was noted amelioration of all symptoms. The patient became afebrile and continued so during the remainder of the hospital course. Fluoroscopy of the heart was normal. Electrocardiograms, however, continued to show sinus rhythm with intermittent nodal tachycardia. The patient was discharged on August 17 on a convalescent leave and was followed by the authors during his convalescence. He continued to show an intermittent nodal tachycardia and was rehospitalized on Aug. 31, 1951. He was started on Pronestyl as a means of controlling the nodal tachycardia.

After Pronestyl was administered for four days in a dosage of 500 mg. every six hours, no change was noted in the dominant nodal rhythm, and it was then decided to use quinidine sulfate orally. On September 5 the patient was given 0.4 Gm. of quinidine sulfate three times a day.

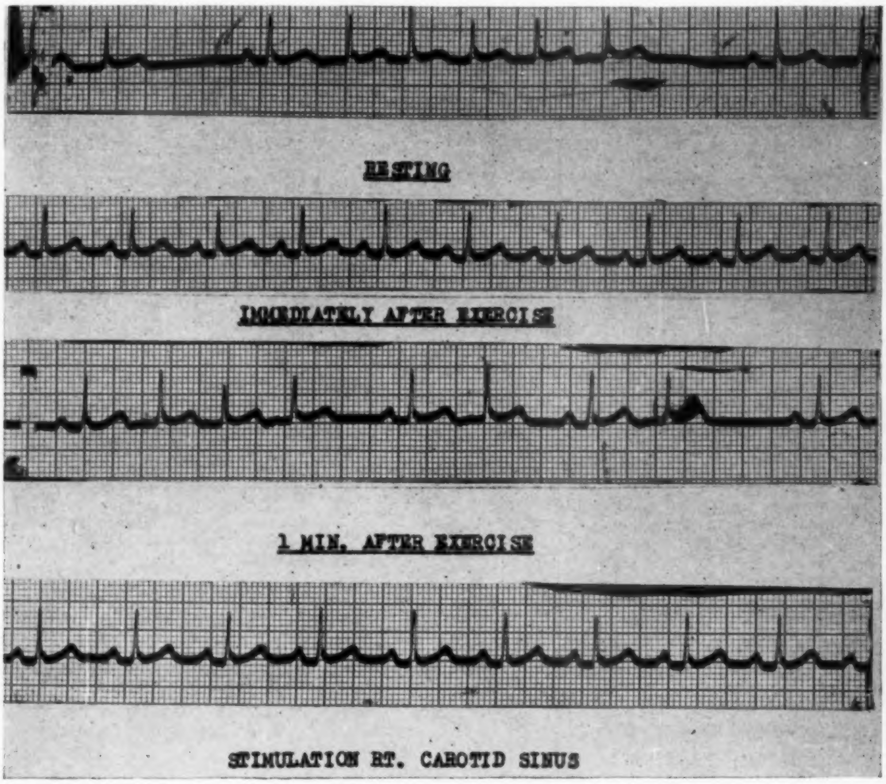

Fig. 2.—This tracing, taken after the administration of quinidine sulfate, shows that exercise and stimulation of the right carotid sinus reverted the abnormal rhythm to normal.

A day later, a repeat electrocardiogram still showed a dominant nodal rhythm. However, after exercise it reverted to a sinus rhythm (Fig. 2), but a minute after exercise it returned to a nodal rhythm. Right carotid sinus pressure was then applied, and the rhythm reverted to normal sinus rhythm. Heretofore, attempts to revert the nodal rhythm to normal sinus rhythm by means of exercise and vagal stimulation had been unsuccessful.

The patient was continued on quinidine sulfate, and repeat electrocardiograms revealed normal sinus rhythm. On September 10 the patient was discharged to the Walter Reed General Hospital for further disposition.

Fig. 3 summarizes the important clinical and laboratory data and the temperature response to Chloromycetin.

COMMENTS

Little is written about the cardiac complications of Rocky Mountain spotted fever, although Harrell,[6] in his excellent review, mentioned that myocardial failure may result from the pathologic process or from overloading the circulation by intravenous therapy. After a review of the literature, we failed to find a cardiac arrhythmia complicating or occurring concomitantly with the disease. To our knowledge, this is the first case of Rocky Mountain spotted fever complicated by an intermittent nodal tachycardia. In their textbooks, both Katz[7] and Friedberg[8] stated that persistent nodal rhythm is an abnormality indicative of myocardial damage. It may occur in acute infections or in a strategically located small lesion. The exact mechanism of a nodal rhythm is little understood. Whatever the mechanism, the sinus node is apparently depressed, and

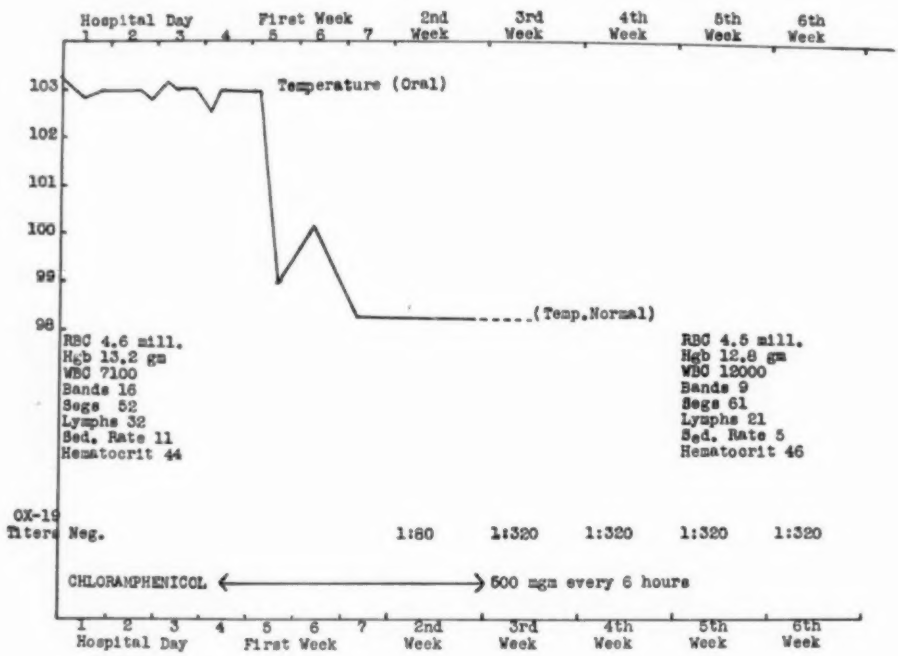

Fig. 3.—Summary of clinical and laboratory data and response to chloramphenicol.

the next specialized tissue to assume the duties of a pacemaker is the atrioventricular node. In this case, electrocardiograms revealed an occasional sinus beat, followed by a period of apparent asystole, with the pacemaker shifted to the atrioventricular node. Once it reached the atrioventricular node, it occasionally migrated within from the upper to the middle to the lower parts of the node. A careful study of the electrocardiogram in Fig. 4, Lead II, shows the first labeled P wave after a sinus beat, occurring 0.12 second before the QRS, indicating that the pacemaker is in the upper part of the atrioventricular node. The next complex shows that there is no P wave, indicating that the pacemaker is probably in the middle of the node, discharging to the sinus and the ventricle

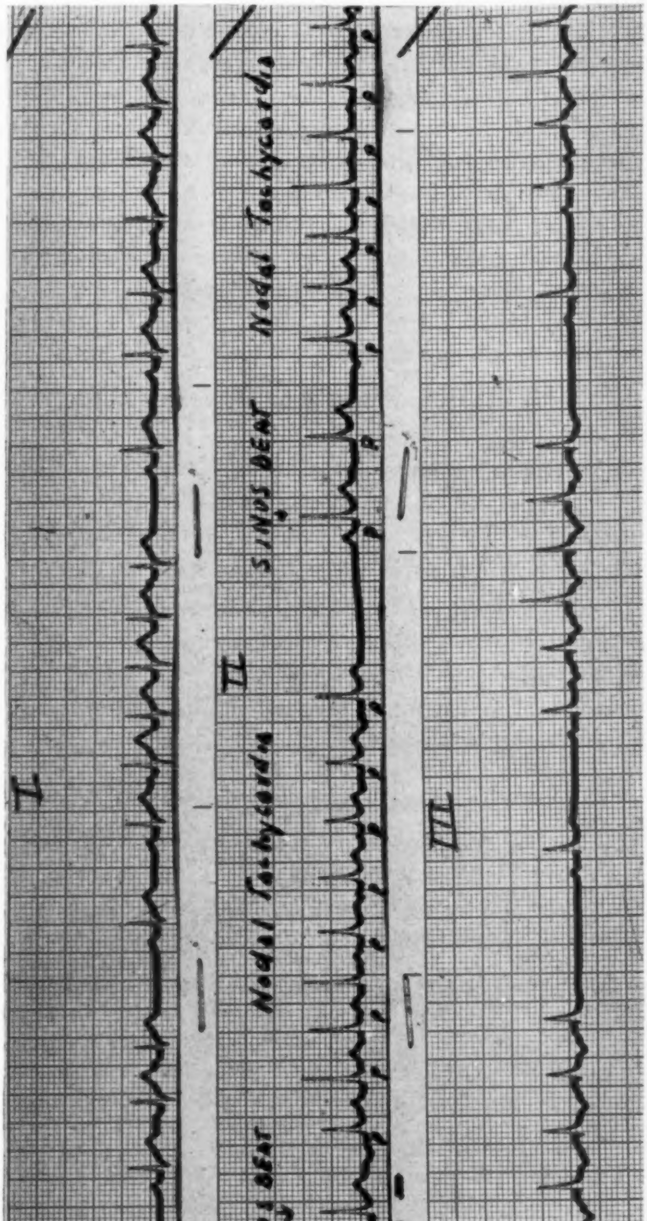

Fig. 4.—This tracing illustrates sinus beats followed by intermittent nodal tachycardia with the pacemaker wandering in the atrioventricular node. The first labeled P wave occurs 0.12 second before QRS. The second labeled P wave occurs in the QRS, and the third labeled P wave follows QRS.

simultaneously. In the third period we see the P wave following the QRS complex, indicating that the pacemaker is in the lower part of the node, having discharged the ventricle first.

The lesions of Rocky Mountain spotted fever in the myocardium, when they occur, are usually small areas of interstitial infiltrations, with some inflammatory reaction, usually related to the smallest arterioles or to the capillaries. It is difficult to say in the case we are presenting whether lesions typical of Rocky Mountain spotted fever occurred near the sinus node, or whether the sinus node was depressed through a vagal effect from the acute inflammatory process. It is our feeling, however, that the disease was instrumental in producing this abnormal rhythm.

SUMMARY AND CONCLUSIONS

1. A patient with Rocky Mountain spotted fever with intermittent nodal tachycardia is presented.

2. A diagnosis of Rocky Mountain spotted fever was established by the clinical course of the disease. This included a history of tick bite, a maculopapular rash, and a rising titer of agglutinations for Proteus OX19.

3. The patient made a dramatic clinical response to Chloromycetin, becoming afebrile within twenty-four hours after initiation of therapy.

4. A dominant intermittent nodal rhythm accompanied the disease and was present long after clinical recovery.

5. The abnormal rhythm was finally abolished, and a normal sinus rhythm was obtained with quinidine sulfate.

REFERENCES

1. Pincoffs, M. C., Grey, E. G., Lister, L. M., Woodward, T. E., and Smadel, J. E.: The Treatment of Rocky Mountain Spotted Fever With Chloromycetin, Ann. Int. Med. **29**:656-663, 1948.
2. Ross, Sidney, Schoenbach, E. B., Burke, F. G., Bryer, M. S., Rice, E. G., and Washington, J. A.: Aureomycin Therapy of Rocky Mountain Spotted Fever, J. A. M. A. **138**:1213-1216, 1948.
3. Cooke, Crispin: Rocky Mountain Spotted Fever Treated With Aureomycin, J. A. M. A. **138**:885, 1948.
4. Havens, Fred Z., Jr., and Stickney, J. Minott: Rocky Mountain Spotted Fever Successfully Treated With Aureomycin: Report of Case, Proc. Staff Meet., Mayo Clin. **25**:338-342, 1950.
5. Parker, Robert T., Bauer, Robert E., Lister, Leonard M., Woodward, Theodore E., and Hall, Howard E.: Further Experience in the Treatment of Rocky Mountain Spotted Fever With Chloramphenicol, Am. J. Med. **9**:308-314, 1950.
6. Harrell, George T.: Rocky Mountain Spotted Fever, Medicine **28**:333-370, 1949.
7. Katz, Louis N.: Electrocardiography, Philadelphia, 1946, Lea & Febiger, p. 535.
8. Friedberg, Charles K.: Diseases of the Heart, Philadelphia, 1949, W. B. Saunders Company, p. 244.

CONGENITAL TRICUSPID ATRESIA

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Several recent reports[1,2] have confirmed the rarity of the lesion and the brevity of life in congenital tricuspid atresia. Taussig[3] stated that "most infants die before one year of age." The oldest case appears to be that of a 5-year-old child reported by Kühne.[4] The following case is added to the literature since the patient lived to an older age than any previously reported patient. It is interesting that her supposedly identical twin had no congenital anomalies.

CASE REPORT

W. P., a 6-year-old white girl, was admitted to Roper Hospital on Nov. 6, 1950, because of convulsions. The child was one of twin girls delivered uneventfully and considered normal at birth. At 5 months of age cyanosis was first observed, and it was recognized that the patient had a heart murmur. Intermittent cyanosis had been present since, but general health was comparable to that of the normal twin except for retarded physical development evident mostly during the past year. Until that time, the twins were identical in all physical features, and cyanosis was the main helpful distinguishing characteristic.

Ten days prior to admission, the patient was found lying on the floor in an extremely cyanotic and exhausted state. She was treated with oxygen and penicillin and responded promptly but two days later had a generalized convulsive seizure leaving her again in the clinical state previously described. Nausea and vomiting and a third convulsion followed, and the patient was transferred to Roper Hospital.

Physical examination revealed a small but well-developed and well-nourished white girl who was lethargic but cooperative. Temperature was 100° F. There was moderate cyanosis of the mucous membranes and skin, and there was clubbing of the nail beds. The chest was clear. The heart was enlarged with the point of maximum apical intensity in the fifth intercostal space just outside the left mid-clavicular line. There was a loud, harsh Grade 3 systolic murmur heard over the entire precordium which was transmitted to the back and heard loudest in the third intercostal space to the left of the sternum. No thrills were palpable. There were no other murmurs. The liver edge was palpable 2 cm. below the right costal margin.

An electrocardiogram revealed left axis deviation with left heart strain in a horizontal heart. The hemoglobin was 18 Gm., and the red blood count was 7 million. The white blood count was 17,500 with 87 per cent polymorphonuclear cells. Fluoroscopy of the heart revealed no definite chamber enlargement but a prominent pulmonary conus.

The clinical impression was that this patient had a variant of the tetralogy of Fallot with probable tricuspid stenosis and underdevelopment of the right ventricle. It was felt that the convulsions were due to small cerebral thromboses secondary to hemoconcentration and cerebral anoxia. With cardiac surgery contemplated, catheterization of the right side of the heart was attempted on Nov. 8, 1950, after the patient had been placed on prophylactic penicillin at the time

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Fig. 1.—Persistent ostium primum (viewed from right auricle).

Fig. 2.—Hypoplasia of right ventricle and interventricular septal defect.

of admission. The catheter could be passed only a few centimeters into the antecubital vein of the left arm, and the procedure was discontinued because of extreme spasm of the veins. Penicillin was stopped the next day, and the temperature rose to 101.6° F. The patient remained lethargic and anorexic, and penicillin was restarted. On Nov. 15, 1950, a blood culture was reported as growing nonhemolytic streptococci. It was now felt that the patient had subacute bacterial endocarditis. On Nov. 18, 1950, the temperature rose to 106° F., accompanied by a generalized convulsive seizure. Papilledema was observed for the first time. Respirations ceased, but life was maintained by means of a respirator with electrocardiograms showing normal sinus rhythm for some ten hours before cardiac action ceased.

At time of death, it was felt that vegetations in the heart had thrown off septic emboli to the brain with development of a brain abscess.

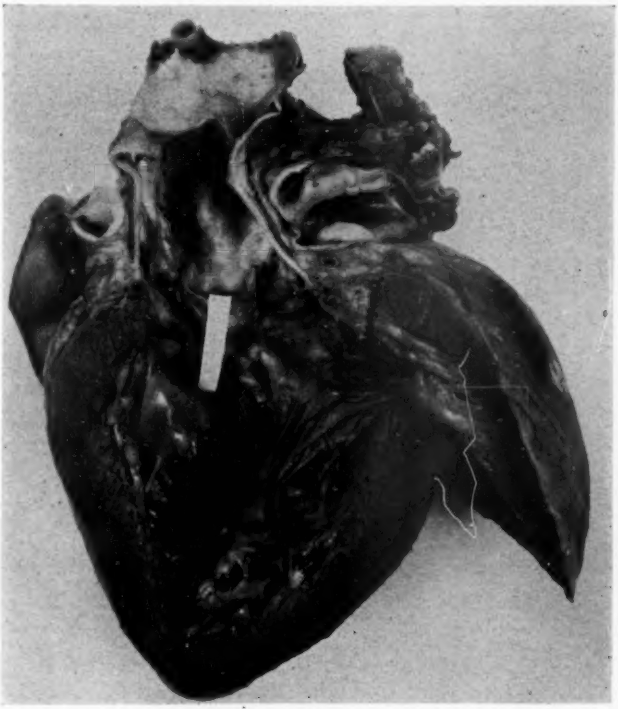

Fig. 3.—Interventricular septal defect (viewed from left ventricle).

Autopsy findings revealed a large brain abscess in the frontoparietal region, atresia of the tricuspid valve, but no evidence of subacute bacterial endocarditis. Culture from the brain abscess showed *Pseudomonas aeruginosa*. The heart weighed 100 grams and showed smooth, glistening endocardial surfaces. There was an interauricular septal defect, apparently ostium primum, which measured 1 by 0.6 cm. (Fig. 1). There was no direct communication between the right auricle and the right ventricle. The right ventricle was a roughly tubular shaped chamber 4 cm. in length and 1.2 cm. in diameter (Fig. 2). Its wall varied from 0.1 to 0.2 cm. in thickness. The circumference of the pulmonary valve measured 3.5 cm. The left ventricle measured 5 by 2 cm., and the myocardium was 0.8 cm. in thickness. The aortic valve ring was 3.5 cm. in circumference. Just inferior to the aortic ring there was a slitlike opening in the interventricular septum 1 cm. in length and less than 0.2 cm. in greatest width which communicated with the right ventricle (Fig. 3). Except for the absence of the tricuspid valve, no valvular defects were noted. The intima of the pulmonary artery and aorta showed surface dimpling at the level of the ductus arteriosus, but this structure had been obliterated and closed.

REFERENCES

1. Sommers, S. C., and Johnson, J. M.: Congenital Tricuspid Atresia, AM. HEART J. **41**:130, 1951.
2. Kroop, I. G.: Congenital Tricuspid Atresia, AM. HEART J. **41**:549, 1951.
3. Taussig, Helen B.: Congenital Malformations of the Heart, New York, 1947, Commonwealth Fund, p. 97.
4. Kühne, Marie: Ueber zwei Fälle kongenitaler Atresie des Ostium venosum dextrum, Jahrb. f. Kinderh. **63**:235, 1906.

COARCTATION OF THE AORTA COMPLICATED BY DISSECTING ANEURYSM IN PREGNANCY: REPORT OF A CASE WITH SURVIVAL, STUDIED BY ARTERIOGRAPHY

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THE combination of pregnancy and coarctation of the aorta, while unusual, can hardly be considered rare. To date there are reports in the literature of forty-three such cases.[1,2,5] It is of interest to note, however, that the situation was complicated by dissecting aneurysm of the aorta in only four of these cases.[2,8-10] In only one was the diagnosis made ante mortem, and none lived more than a few days after dissection had occurred.

We are therefore prompted to make this report of a young white woman, 28 years old, now living, who had coarctation of the aorta and who developed dissecting aneurysm of the aorta and subclavian artery in close association with pregnancy early in 1950, approximately nineteen months prior to this report. The relation between pregnancy and dissecting aneurysm of the aorta and the possible relation between dissection and retrograde angiocardiograms, which were made in this case, are the two most important features of this report.

CASE REPORT

There was a history of migratory polyarthritis and frequent epistaxes in childhood. Slight exertional dyspnea and ankle edema had been noted since that time. The family history was not pertinent. In 1943, at the age of 20 years, she developed a severe toxemia of pregnancy with hypertension (systolic pressure of 200 mm. Hg), dyspnea, edema, albuminuria, and hematuria, which terminated in the delivery of a full-term viable infant. In 1945, at the age of 22 years, she was admitted to the hospital for the first time for nephrolithotomy because of bilateral renal calculi. At that time the blood pressure was 150/90 mm. Hg. There were noted a loud, blowing, precordial systolic murmur, maximum at the apex, and a faint diastolic murmur along the left sternal border. The heart was not enlarged. Following lithotomy, she did well until about six months prior to the second admission on Feb. 20, 1950, at which time she entered the hospital because of dizziness and scotomas associated with sudden movement of the head, blurring of vision, increasing fatigue, and moderate dyspnea. She was two and one-half months pregnant. Examination revealed a blood pressure of 144/76 mm. Hg in the right arm and 160/84 mm. Hg in the left. The blood pressure was variable and was noted as high as 165/100 mm. Hg. No pulsations were noted anywhere below the level of the diaphragm. Radial and brachial pulsations were normal. Pulsations were noted along the lower rib margins posteriorly and along the vertebral margins of the scapulae. The optic fundi showed arteriolar tortuosity. The lungs were clear. Chest roentgenograms revealed the heart to be at the upper limits of normal, with a hypertensive configuration and notching of the ribs. A Grade 3 basilar systolic murmur, loudest over the aortic area,

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unassociated with a thrill, was noted which extended into the base of the neck and interscapular area. No diastolic murmur was heard. The mitral first sound was not remarkable. Laboratory studies revealed normal values. There was no urinary abnormality.

On Feb. 21, 1950, retrograde arterial injection of 50 c.c. of 70 per cent Diodrast was performed via the left common carotid artery. Eight x-ray films were taken at one-second intervals with the patient in the left anterior oblique position. The coarctation was visualized clearly with only a small amount of dye, sufficient to cast a faint shadow, distal to the site of coarctation. The involved segment of the aorta was relatively short with a sharply defined indentation suggesting a diaphragmatic type of obstruction. A well-developed collateral circulation was easily seen. Further comment regarding these films will be made later. The patient seemed to suffer relatively little discomfort following this procedure, and the pain which was noted in and about the neck was not inconsistent with the nature of the procedure.

A cervical dilatation and curettage was performed March 4, 1950.

On March 10, 1950 thoracotomy was performed. The area of coarctation was short and lay just distal to the origin of the left subclavian artery. The aorta below the site of coarctation appeared normal. Above, the vessel was markedly sclerotic, and calcified yellow plaques were easily visible within the vessel wall. Areas of dark blue discoloration were noted at various points. The region of the ligamentum was densely scarred. It was deemed unwise to attempt an end-to-end anastomosis. The first portion of the left subclavian artery was quite rigid and sclerotic, but the more distal portions appeared more nearly normal. The subclavian artery was divided and the distal end ligated. When an attempt was made to swing the proximal segment around to the aorta, it was found to be too rigid to be turned sufficiently to effect an anastomosis. Inspection of the cut end of the subclavian artery revealed that the intima had been dissected away from the media over one-half the circumference of the vessel; the space between the intima and media was occupied by a thrombus which appeared three or four weeks old. Unfortunately, no specimen was obtained for microscopic study. At this point the subclavian artery was ligated, and the procedure was terminated. The postoperative course was uneventful, and the patient was discharged on March 21, 1950. Electrocardiograms made during hospitalization were within normal limits.

Since discharge, the patient has done light housework with little or no distress. More than slight exertion produces precordial discomfort. Headaches have not returned. There is no evidence of cardiac failure. The blood pressure in the right arm eleven months after operation was 220/110 mm. Hg. The electrocardiographic pattern and the character of the murmur have not changed.

COMMENT

A review by Schnitker and Bayer[4] of 141 reported cases of dissecting aneurysm in persons under 40 years of age revealed that one-half of the forty-nine women in the group were pregnant at the time dissection occurred. Dissection was definitely not related to the strain of labor, since in twenty of the twenty-four women the dissection was diagnosed well in advance of labor. Mention is made of the possible relation between medial changes, vascular dissection, and changes in lipid metabolism during pregnancy. It is of interest to note that one-third of the cases reviewed were complicated by distinct narrowing or actual coarctation of the aorta.

The patient described in the present report represents the fifth case of dissecting aneurysm in forty-four reported cases of coarctation of the aorta in pregnancy. Seven of the forty-four subjects died during pregnancy; four of the seven were women who developed dissecting aneurysm. While these represent only a small series, it is difficult to escape the conclusion that pregnancy increases the likelihood of death from aortic dissection, particularly in the presence of coarctation. The studies of Reifenstein and associates[3] indicate that aortic dissection is

responsible for only 18 per cent of the deaths in patients with coarctation, regardless of age or sex.

At this point it should be pointed out that the term "dissection of the aorta" is used advisedly. In Reifenstein's review[3] of 104 autopsied cases of coarctation, attention is called to the paucity of adequate microscopic studies of the aorta, especially of the ascending portion. Medial thinning with necrosis or hyaline degeneration, fibrosis, decrease and fragmentation of elastic fibers, basophilic appearance, and cystic changes are all described. It is unlikely that Erdhein's necrosis (medionecrosis cystica) was the common or typical lesion found in these dissected aortas. On the other hand, there is a deficiency of the media when coarctation is present, and cystic medial necrosis, whenever present and whatever its cause, is found predominantly in the ascending aorta, the commonest site for rupture or "dissection" to occur in coarctation. Atherosclerosis is often minimal or least marked in this region. Schnitker and Bayer's review[4] of aortic dissection in patients under 40 years indicates that Erdhein's necrosis, or medionecrosis cystica, is the primary fault underlying dissecting aneurysm of the aorta per se.

Fig. 1.—Retrograde aortogram taken approximately one second after the dye injection was begun. The site of coarctation is easily visualized. See text for further comment.

The retrograde arteriograms are worthy of special comment. The one-second film (Fig. 1) shows a high concentration of dye in the left common carotid artery between the needle and aortic arch. There was little or no retrograde filling of the aorta proximal to the site of origin of the left common carotid

Fig. 2.—Two-second aortogram showing further aortic and subclavian filling and opacification of the internal mammary artery. The previously smooth filling of the proximal subclavian artery is replaced by an irregular pattern, suggesting turbulence in this area.

Fig. 3.—Three-second aortogram. The carotid shadow is now fainter, indicating that the dye injection has been completed. The turbulent area in the subclavian artery is even more apparent.

artery. The aortic arch between this site and the coarctation is easily visualized on this film, although the contrast is not as marked at this time as in later films. Some dye is faintly visualized distal to the coarctation. The first portion of the left subclavian artery and part of the mid-portion have also been partially opacified by dye. Its S-shaped curvature is smooth, and there is no interruption of the continuity of the vessel wall save for the origin of a small vessel on the superomedial aspect. The two-second film (Fig. 2) shows about the same opacification of the common carotid artery with further retrograde filling of the aorta. The arch proximal to the coarctation is now more completely opacified, and the more distant subclavian artery and several branches are now clearly seen.

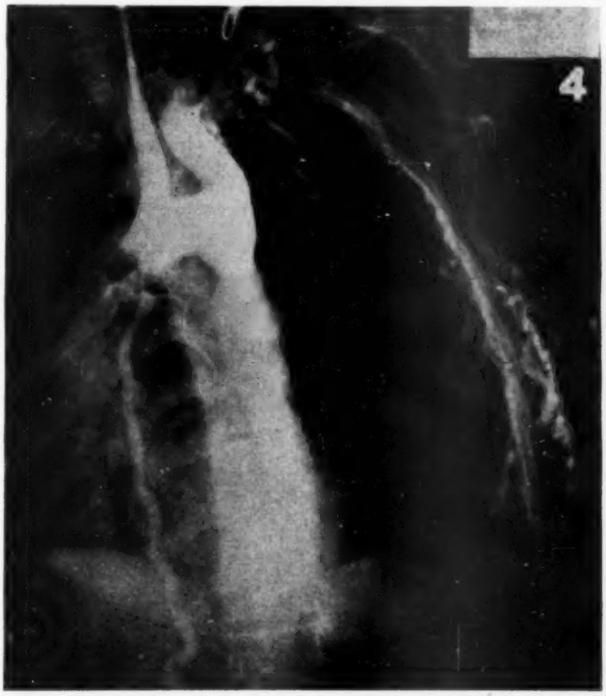

Fig. 4.—Four-second aortogram. The distal subclavian artery has now begun to fade. The turbulent area is virtually free of contrast material, and a rather sharply demarcated dye pattern in this vessel is seen in this and subsequent films.

In addition, a large internal mammary artery is visualized. However, there is seen now in the superior curve of the subclavian artery a gross disruption of the previously uniform pattern, suggesting great turbulence in this area. In the three-second film (Fig. 3) less dye is seen in the carotid artery, indicating that between the two- and three-second films the Diodrast injection had been completed. The subclavian artery is more opacified, and the turbulent or disrupted area is more readily apparent. The internal mammary artery is also more opaque. In the four-second film (Fig. 4) the portion of the subclavian artery distal to the mid-portion of its superior curve has begun to fade; the collateral arteries arising from the subclavian artery are now visible in a greater extent. However, the area of turbulence is relatively free of contrast material, and the first or ascending

portion of the subclavian artery, well opacified, is seen to be rather sharply demarcated in a pattern consistently repeated in the remaining films. In the five-second film (Fig. 5) the carotid artery is less opaque, and tortuous intercostal arteries are seen. The previously mentioned segment of the aortic arch and the first portion of the subclavian artery remain almost precisely as before. It is of great interest to note that while the dye disappeared from the remaining vessels, with the exception of the internal mammary artery, which takes origin from the first portion of the aortic arch, the pattern first noted in the four-second film persisted throughout the remainder of the films. This segment of arch and the first portion of subclavian artery are only slightly, although definitely, less opaque at eight seconds than at four seconds, indicating that outflow of dye from this region is remarkably slow. The persistence of dye in the internal mammary artery, with decreasing concentration visible on close inspection of the five- and eight-second films (Figs. 5 and 6), indicates that dye left this region primarily via the internal mammary artery, and suggests that partial obstruction to outflow of dye from first to second, or mid-portion, of the subclavian artery developed between the one-second and four-second films, since the first three arteriograms show good concentration of dye in this vessel, and the one-second film suggests no impediment to flow.

This interpretation of these arteriograms will undoubtedly be questioned by some. Turbulence, lamellar flow, and axial streaming may serve to produce effects of an otherwise inexplicable and unpredictable nature. Nevertheless, it is rather difficult to escape the conclusion that blood flow along the first portion of the subclavian artery was or became partially obstructed. The nature of such obstruction, if indeed present, is not apparent from the roentgenograms. The possibility exists that an intimal tear developed, in association with the subintimal dissection, which ballooned out and partially obstructed the lumen of the subclavian vessel. The smooth appearance of the subclavian artery on the one-second film suggests that such tearing and subsequent ballooning may have occurred between this and subsequent films. If such is the case, then either the incision in the carotid artery or the rapid injection of 50 c.c. of dye into diseased vessels already subjected to abnormally high pressures or both may have sufficed to produce intimal tearing and/or intramural dissection. The importance of these considerations will be realized if they give us pause when considering procedures requiring the interruption of the integrity of a vessel wall of the caliber and importance of the carotid artery or the rapid injection of relatively large volumes of materials against a high head of pressure in a diseased vascular system.

SUMMARY AND CONCLUSIONS

This is the first report of a case of coarctation of the aorta in pregnancy, complicated by dissecting aneurysm, in which the patient is living and relatively symptom free more than one year following diagnosis and exploratory thoracotomy.

When death due to cardiovascular complications occurs during pregnancy or shortly after delivery in women with coarctation, the commonest cause of death

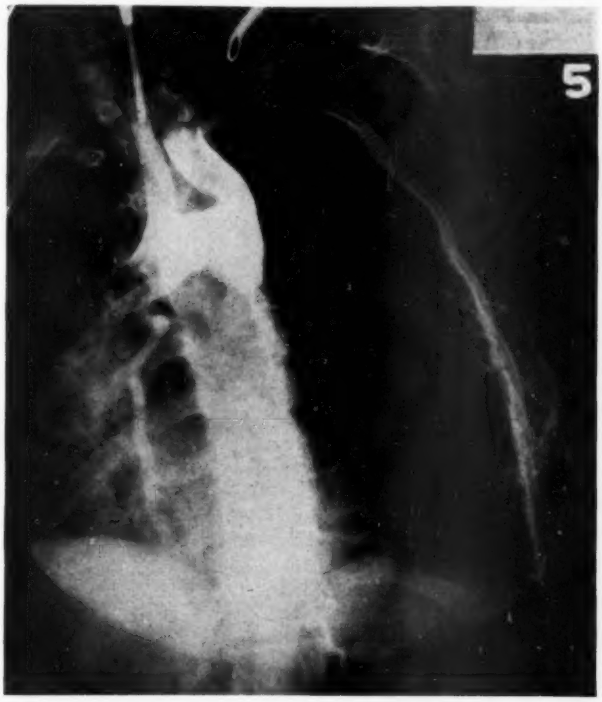

Fig. 5.—Five-second aortogram. The first portion of the aortic arch and subclavian artery are about as before. The dye pattern in the subclavian artery remains as before.

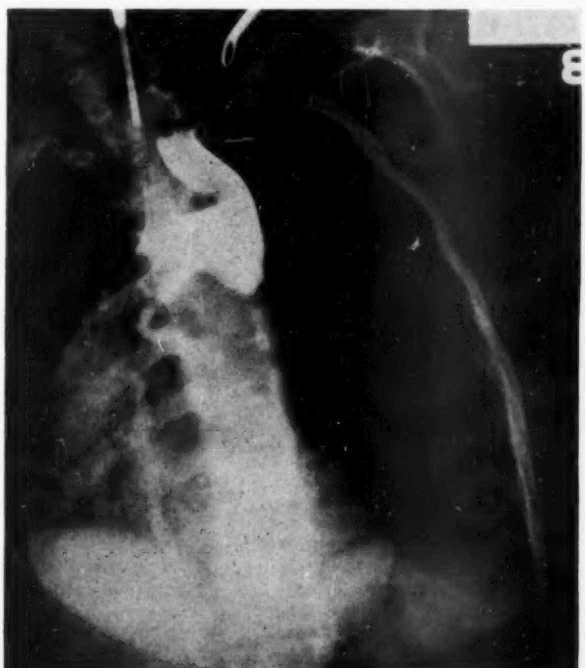

Fig. 6.—Eight-second aortogram. The dye pattern in the subclavian artery is the same as before. The proximal subclavian artery and aortic arch remain well opacified.

is dissection of the aorta. An earlier review is cited which indicates that pregnancy may predispose to aortic dissection, particularly in the presence of a congenital anomaly of the aorta.

Retrograde angiograms are presented and discussed. The question is raised as to whether the retrograde injection of contrast material in this instance might have produced intimal tearing with dissection, and a note of caution is sounded regarding this method of study in such cases.

REFERENCES

1. Baber, M. D., and Daley, D.: Coarctation of the Aorta With Pregnancy, J. Obst. & Gynec. Brit. Emp. **54**:91-96, 1947.
2. Kinney, T. B., Sylvester, R. E., and Levine, S. A.: Coarctation of the Aorta, Dissection of the Aorta and Pregnancy in Females, Am. J. M. Sc. **210**:725-732, 1945.
3. Reifenstein, G. H., Levine, S. A., and Gross, R. E.: Coarctation of the Aorta, AM. HEART J. **33**:146, 1947.
4. Schnitker, M. A., and Bayer, C. A.: Dissecting Aneurysm of the Aorta in Young Individuals Particularly in Association With Pregnancy With Report of a Case, Ann. Int. Med. **20**:486, 1944.
5. Mendelson, C. L.: Pregnancy and Coarctation of the Aorta, Am. J. Obst. & Gynec. **39**:1014-1021, 1940.
6. Burwell, C. S., Strayhorn, W. D., Flickenger, D., Corlette, M. B., Bowerman, E. P., and Kennedy, J. A.: Circulation During Pregnancy, Arch. Int. Med. **62**:979, 1938.
7. Thompson, K. J., Reid, D. E., and Cohen, M. E.: Studies on the Circulation in Pregnancy, Am. J. M. Sc. **198**:665, 1939.
8. Billinghurst, W. B.: Coarctation of the Aorta as an Obstetrical Complication, Brit. M. J. **1**:303, 1943.
9. Strassman, G.: Beitr. z. gerichtl. Med. **5**:95, 1922 (as quoted by Mendelson).
10. Katz, H.: Arch. f. Gynäk. **115**:283, 1922 (as quoted by Mendelson).

COMPLETE DEXTROPOSITION OF THE AORTA, PULMONARY STENOSIS, INTERVENTRICULAR SEPTAL DEFECT, AND PATENT FORAMEN OVALE

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THE following case represents an unusual congenital malformation of the heart. Since it has been possible to correlate the clinical and physiologic findings with the autopsy findings, the case is reported in detail.

CASE REPORT

R.B., a 19-year-old man, was admitted to the Medical Department B on Nov. 14, 1950, because of congenital heart disease and congestive heart failure. A heart lesion had been diagnosed at birth. From an early age he tired very easily, was unable to run as other children, and had a bluish color of the face and extremities. He frequently experienced spells of dizziness. In childhood the patient had measles and repeated attacks of tonsillitis. Seven years before the present admission he had rheumatic fever.

The patient attended school until the autumn of 1949 when he was found unconscious. At that time swelling of the ankles was noted and the liver was found to be enlarged. After treatment in a hospital the edema disappeared, but when he returned home the edema recurred and he was rehospitalized. Following frequent mercurial injections he again improved and this treatment was continued at home up to the present. During the last year he was bedridden most of the time because of heart failure.

On admission the patient was in a bad nutritional state. The facies was mongoloid and the skin had a bluish-red tint and there was marked cyanosis of the lips and the upper and lower extremities. The cyanosis was equally distributed. Rapid venous pulsations were visible on both sides of the neck.

The chest wall on the left side appeared more prominent than on the right. Breath sounds and vocal fremitus were normal over both lungs. The pulse was regular, equal, of small volume, and the rate was 84. The blood pressure was 110/70 mm. Hg in both arms. The apex beat was felt in the sixth intercostal space in the midaxillary line; a systolic thrill was felt over the whole precordium with maximum intensity in the second left intercostal space. On percussion the right heart border was found 1 cm. to the right of the sternum, the upper border was in the third intercostal space, and the left border was in the midaxillary line of the sixth intercostal space. The heart sounds were clear; splitting of the first sound was heard; the second aortic sound and the pulmonary sound were of the same intensity. A systolic murmur was heard over the entire precordium with the maximum intensity over the second left intercostal space.

The abdomen was symmetrical. Shifting dullness was present. The liver was palpable in the mid-sternal line 5 cm. below the costal margin and was pulsating. The spleen was not palpable.

Both knee and ankle joints were moderately swollen. There was marked clubbing of fingers and toes. Bilateral ankle edema was present. Pulsations of the dorsalis pedis artery were felt on both sides.

From the Rothschild Hadassah University Hospital, Jerusalem, Israel.
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The red cell count was 7,390,000 per c.mm; the hemoglobin was 22.8 Gm. per cent; hematocrit 74. The urine showed 1 per cent albumin. The blood urea was 60 mg. per cent.

X-ray Examination.—In the posteroanterior position (Fig. 1), the heart was enlarged in all directions; the shadow of the aorta was slightly enlarged, especially to the right. The pulmonary segment showed a slight concavity. The third arch of the left heart border was prominent. The barium-filled esophagus showed a displacement to the left at the level of the aortic arch. There were decreased hilar and pulmonary markings with abnormally clear lung fields. In the right anterior oblique position the retrosternal space was obliterated, and there was a slight overlapping of the posterior heart border over the spine. The barium-filled esophagus did not deviate in its lower third. In the left anterior oblique position the heart was markedly enlarged anteriorly and posteriorly.

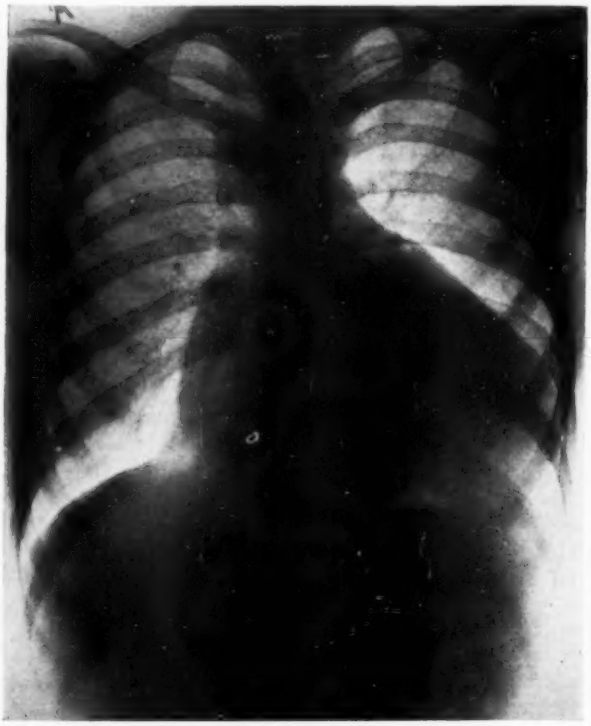
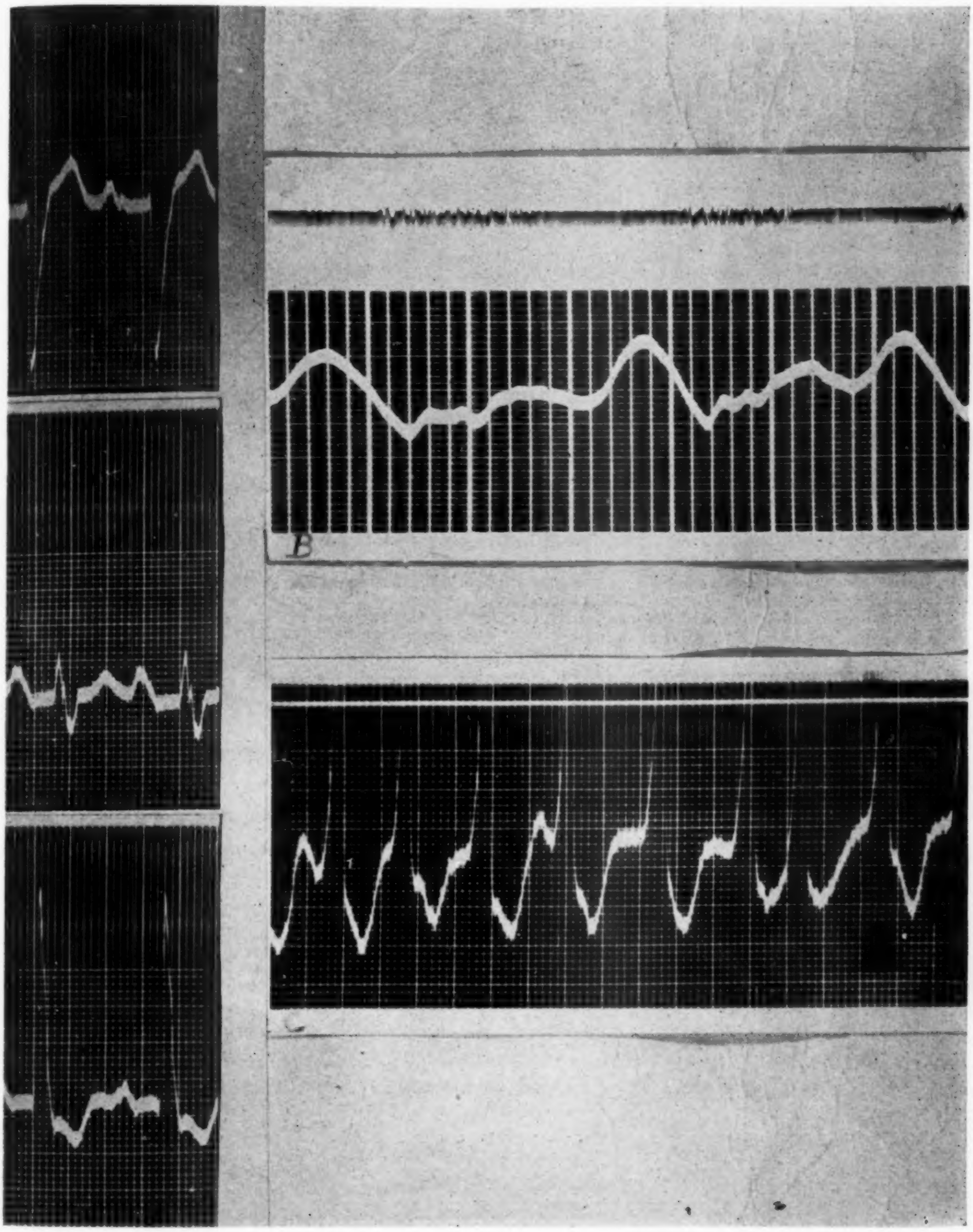


Fig. 1.—For description, see text.

X-ray Resume'.—Congenital heart disease; enlargement of the heart, especially of the right ventricle and the right atrium; right aortic arch; and decreased pulmonary vascular markings.

The electrocardiogram (Fig. 2,*A*) showed a regular sinus rhythm, notched and peaked P waves, and a P-R interval of 0.26 second. The QRS was broadened (0.12 second) and slurred with a marked S wave in Lead I and a prominent R in Lead III. The T wave in Lead I was upright and in Lead III it was inverted. The precordial leads showed a tall R and an inverted T in Lead V_1 and a deep S in Lead V_5. This electrocardiogram was interpreted as indicating atrial hypertrophy, delayed atrioventricular conduction, and right ventricular hypertrophy. Venous pulse tracings from the liver showed atrial waves of high amplitude; a simultaneously recorded phonocardiogram of the apex region demonstrated a prolonged systolic murmur (Fig. 2,*B*).

Physiological Studies.—The results of the right heart catheterization are summarized in Table I. The results of the exercise tests are summarized in Tables II and III.



B.

A.

C.

Fig. 2.—*A*, Standard limb leads showing the pattern of right ventricular hypertrophy. *B*, The liver sphygmogram and simultaneously recorded phonocardiogram show presystolic venous pulse and prolonged systolic murmur. *C*, Run of ventricular tachycardia during catheterization.

TABLE I. CARDIAC CATHETERIZATION DATA

LOCALIZATION OF CATHETER TIP	PRESSURE CM. SALINE*	OXYGEN CONTENT VOL. %†	REMARKS
Peripheral vein		4.9	
Sup. vena cava	18.5	5.1	
Right atrium‡	16.0, 18.5	10.8, 11.0	
Right ventricle	55.0	11.1	Ventricular pulsations in the manometer Ventricular tachycardia§
Right or left ventricle‖	45.0	12.5	

Arterial 0_2 content (brachial artery)	15.6 vol. %¶
Arterial 0_2 capacity	29.2 vol. %
Arterial 0_2 saturation	53.5%

*Pressure was measured with a saline manometer; the auricular level was estimated 5 cm. below the sternocostal junction of the fourth rib.

†The oxygen content was determined by the method of Van Slyke and Neill.[6]

‡The two values were obtained at different localizations of the catheter tip.

§A run of ventricular tachycardia (Fig. 2, *C*) developed when the catheter was in the right ventricle. Normal rhythm was re-established after changing of the position of the catheter tip.

‖It could not be decided with certainty whether the catheter was still in the right ventricle or had passed into the left through a septal defect.

¶The aterial sample was taken the day before the cardiac catheterization.

TABLE II. BLOOD OXYGEN CONTENT AT REST AND AFTER EXERCISE*

	BEFORE EXERCISE (VOL. %)	AFTER EXERCISE (VOL. %)
Arterial blood	15.6	11.5
Venous blood (peripheral)	2.6	1.2

*Because of the inability of the patient to perform a step test he was made to change his position from supine to prone fifteen times during a period of two minutes.

TABLE III. OXYGEN CONSUMPTION PER LITER OF VENTILATION AT REST AND DURING EXERCISE*†

AT REST	DURING EXERCISE
22 ml. 0_2 per L. vent.	8.6 ml. 0_2 per L. vent.

*The patient, in supine position, performed cycling movements with the legs against manually applied resistance.

†These measurements were obtained with a Benedict Roth respirometer provided with an automatic ventilation recorder.

The preceding data demonstrate that exercise caused a marked drop in arterial oxygen content and a very pronounced decrease in the oxygen consumption per liter of ventilation.

Additional lung function studies are reported in Table IV. They show a marked reduction in the vital capacity and the maximum breathing capacity.

TABLE IV. LUNG FUNCTION STUDIES

Tidal air	468 ml.
Reserve air	330 ml.
Complementary air	1390 ml.
Vital capacity	1900 ml.
Maximum breathing capacity	50.1 L./min.

Interpretation of Physical and Laboratory Findings.—In the interpretation of the hemodynamics the authors were led mainly by the results of the cardiac catheterization. The much higher oxygen content of the right atrial blood as compared with the blood from the superior vena cava indicates an admixture of arterial blood in the right atrium. The absence of a systolic venous pulse in the liver sphygmogram makes it probable that the admixture of arterial blood in the right atrium originated mainly from the left atrium and that it was not due to regurgitation from the right ventricle through a severely insufficient tricuspid valve. In the right ventricle the oxygen content was almost the same as in the right atrium. The higher oxygen content of 12.5 volume per cent which was found when the catheter was passed farther down and to the left can be explained in two different ways. Either the catheter had approached a ventricular septal defect but still remained in the right ventricle, or the catheter had passed through such a defect into the left ventricle. The elevated right atrial pressures of 16 and 18 cm. saline may be explained by the congestive heart failure, or a tricuspid stenosis, or by increased filling of the right atrium by blood coming from the left atrium. Each one of these three mechanisms could be responsible for the presystolic liver pulse. The elevated right ventricular pressure may have been due to several causes or a combination of them: (a) congestive failure, (b) overriding of the aorta, (c) pulmonary stenosis. The x-ray finding of clear lung fields in the presence of congestive heart failure is consistent with pulmonary stenosis. Additional support for the latter assumption was obtained from the exercise test which showed an extreme decrease of the oxygen consumption per liter of ventilation during exercise (Table II). Also the arterial oxygen content dropped markedly after exercise which indicated an increase in the right to left shunt, a finding characteristic of pulmonary stenosis with septal defect. A right aortic arch was diagnosed because of the indentation of the esophagus on the right side.

On the basis of these findings the presumptive diagnosis was made of a congenital malformation of the heart consisting of an interatrial septal defect, pulmonary stenosis, and right aortic arch. The existence of an interventricular septal defect, an overriding aorta, and tricuspid stenosis was considered.

Course in Hospital.—The congestive heart failure gradually increased and failed to respond to digitalis and mercurial diuretics. Two weeks after the patient's admission a massive hemorrhage from the lungs occurred and caused the death of the patient.

Post-mortem Examination.—A summary of the pertinent anatomic findings was as follows: Complete dextroposition of the aorta; stenosis of the pulmonary artery and a displacement of this vessel toward the left; interventricular septal defect of the membranaceous portion; obliquely patent foramen ovale; stenosis and insufficiency of the mitral and tricuspid valves with acute and healed verrucous valvulitis of tricuspid, mitral, and aortic valves; dilatation of all cardiac chambers and hypertrophy of right atrial and right and left ventricular walls; bilateral widespread hemorrhages of both lungs; and marked chronic passive congestion of the liver with central necrosis and periportal fibrosis.

Measurements (circumferential): Tricuspid valve, 9.5 cm.; pulmonary valve, 3.3 cm.; mitral valve, 7.2 cm.; aortic valve, 7.0 cm.; right ventricular wall at origin of aorta, 0.9 cm., and at apex, 0.9 cm.; left ventricular wall at level of mitral valve, 0.9 cm., and at apex, 0.9 cm.; right and left atrial walls, 0.1 to 0.2 cm.; interventricular septal defect 1.7 cm. anteroposteriorly and 1.2 cm. caudocephalad.

Fig. 3.—Photograph of autopsy specimen.

At the time of autopsy the heart was found to be markedly enlarged. The right atrium and auricle together were as large as both ventricles and the former occupied approximately four-fifths of the presenting surface. The axis of the heart was transverse and slightly rotated posteriorly.

The aorta arose from the right ventricle to the right of the pulmonary artery and slightly cephalad. The pulmonary artery originated in part from the interventricular septum, its left wall arising from the septum; the remainder of the vessel arose from the right ventricle. It had a valve with two leaflets, one situated posteriorly and the other toward the left and anteriorly.

The foramen ovale was obliquely patent to a probe. Without distension of the atrial chambers the orifice was closed. However, with slight to moderate dilatation of these chambers, the foramen became patent. The coronary arteries showed a normal distribution.

COMMENT

In the case presented, both the aorta and the stenotic pulmonary artery originate from the right ventricle. It differs from a classic tetralogy of Fallot

in that the aorta does not arise from the left ventricle and partially override the ventricular septum, but is transposed and arises entirely from the right ventricle. Thus the right ventricle serves as a "double outlet ventricle." According to the classification of Lev and Volk[4] this malformation is a type of partial transposition of the Fallot type.

The pertinent signs in this case were: cyanosis since birth, clubbing, dilatation of the heart, a harsh systolic murmur over the entire precordium, a clear second pulmonary sound of normal intensity, a presystolic liver pulse, and marked congestive heart failure. The x-ray examination showed a markedly enlarged heart with clear lung fields. The electrocardiogram showed atrial hypertrophy and right ventricular hypertrophy.

It is of interest to correlate the results of the clinical examinations with the anatomic findings.

The extreme cyanosis since birth is well explained by the origin of the aorta from the right ventricle. That pulmonary stenosis played an additional part in the causation of the cyanosis is indicated by the very clear lung fields.

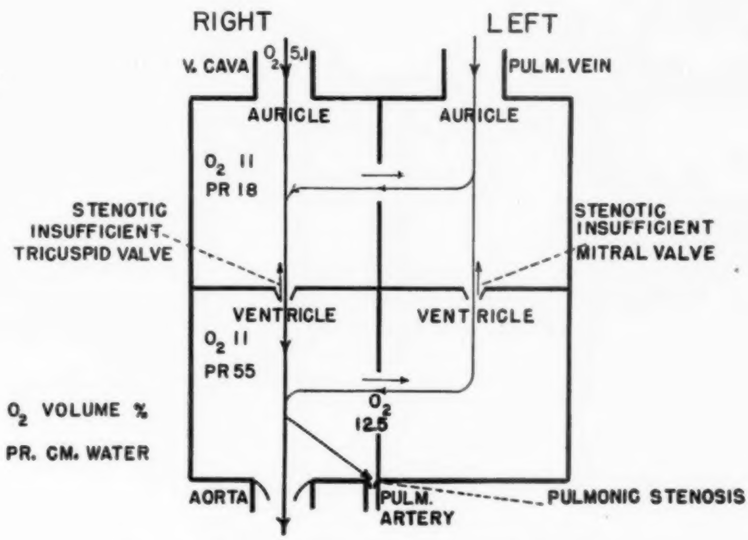


Fig. 4.—Schematic illustration of the circulation course.

The interventricular septal defect, the pulmonary stenosis, as well as the mitral insufficiency, all may have contributed to the formation of the systolic murmur, although the harsh character of the murmur, as well as the thrill, point to the pulmonary stenosis as the main cause. The absence of any diastolic murmur is remarkable considering the presence of tricuspid and mitral stenosis. The clear pulmonic sound of a normal intensity in the presence of a severe pulmonary stenosis might seem unexpected but is in keeping with the experience of other authors (Baker et al.[1] and Silber et al.[5]). The presystolic liver pulse is well explained by the tricuspid stenosis although, according to the recent studies of Grishman and associates,[3] the extreme dilatation of the right atrium alone may

be sufficient to cause this phenomenon. There was a good correlation between the electrocardiographic signs of auricular and right ventricular hypertrophy and the anatomic findings.

The interpretation of the circulatory measurements was thus in agreement with some of the post-mortem findings since pulmonary stenosis and patent foramen ovale were diagnosed and the existence of an interventricular septal defect, overriding aorta, and tricuspid stenosis were considered. The reconstruction of the circulation on the basis of the functional and anatomic findings is shown in Fig. 4. As shown in this diagram the oxygenated blood coming through the pulmonary veins to the left atrium is shunted to the right atrium and then passes with the main stream of the venous blood through the stenotic tricuspid valve into the right ventricle. The larger part of the right ventricular blood enters directly into the aorta which is completely dextroposed, while a smaller amount of this blood flows into the stenotic pulmonary artery. The presence of a severely stenotic mitral valve probably raises the pressure in the left atrium and thus might be responsible for the shunting of a considerable amount of arterial blood from the left atrium through the patent foramen ovale, similarly as it is known to occur in Lutembacher syndrome. Part of the left atrial blood passes the stenotic mitral valve and, having passed through the interventricular septal defect, enters the pulmonary artery and the aorta. No anatomic data concerning the role of collaterals from the bronchial arteries to branches of the pulmonary artery were obtained.

SUMMARY

The clinical, physiologic, and pathologic findings in a 19-year-old boy with congenital heart disease and acquired valvular disease are reported.

The congenital anomaly consisted of complete dextroposition of the aorta, pulmonary stenosis, interventricular septal defect, and patent foramen ovale.

The authors' thanks are due to Dr. M. Lev, of the University of Illinois, for his kind advice, and to Mrs. K. Galevsky for her technical assistance.

ADDENDUM

Since this paper was submitted for publication, Drs. M. Campbell and S. Suzman have reported in their review, Transposition of the Aorta and Pulmonary Artery (Circulation **4**:329, 1951), a very similar case (Case No. 9) to the one reported by us.

REFERENCES

1. Baker, Charles, Brock, R. C., Campbell, M., and Suzman, S.: Morbus Coeruleus, Brit. Heart J. **11**:170, 1949.
2. Bing, R. J.: The Physiology of Congenital Heart Disease, Nelson's Loose Leaf Medicine, p. 423, 1950.
3. Grishman, A., Kroop, I. G., and Steinberg, M. F.: Presystolic Pulsations of the Liver in the Absence of Tricuspid Disease, Am. Heart J. **40**:731, 1950.
4. Lev, M., and Volk, B. W.: The Pathologic Anatomy of the Taussig-Bing Heart: Riding Pulmonary Artery, Bull. Internat. A. M. Mus. **31**:54, 1950.
5. Silber, E. N., Prec, O., Grossman, N., and Katz, L. N.: Dynamics of Isolated Pulmonary Stenosis, Am. J. Med. **10**:21, 1951.
6. Van Slyke, D. D., and Neill, J. M.: The Determination of Cases by Vacuum Extraction and by Manometric Measurements, J. Biol. Chem. **61**:523, 1924.

CONGENITAL ANEURYSM OF THE MEMBRANOUS PORTION OF THE VENTRICULAR SEPTUM: REPORT OF TWO CASES

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Aneurysms of the ventricles of the heart may be acquired or congenital. Aneurysms of the membranous portion of the ventricular septum are usually considered to be in the latter group. It is the purpose of this report to record two additional cases of this anomaly observed recently at necropsy. In one of these cases the clinical course of the patient, who was observed for ten years, was characterized by extreme cardiac irritability. While aneurysms of the membranous portion of the ventricular septum are usually unassociated with clinical manifestations, it is probable that in one of these cases the aneurysm was of clinical significance.

CASE REPORTS

Case 1.—*Clinical Features.* The patient was an 18-year-old white girl. Mongolian idiocy had been diagnosed during the first year of her life. In adolescence, tuberculosis had developed. The patient had not been observed or examined by the authors while she was alive. Death occurred shortly after admission to Mound Park Hospital, St. Petersburg, Fla., on Dec. 27, 1948.

Pathologic Features.—At necropsy, the following anatomic diagnoses were made: pulmonary tuberculosis (bilateral), congenital aneurysm of the membranous portion of the ventricular septum, and tuberculous enteritis.

The body weighed an estimated 90 pounds (about 41 kg.) and measured 55 inches (about 140 cm.) in length. The pertinent findings were confined to the heart. In the ventricular septum there was an aneurysm (Fig. 1,*A*) with its orifice measuring 1.4 cm. in diameter. This was located in the upper third of the septum at the junction of the muscular portion of the ventricular septum with the membranous portion. It was located immediately beneath the posterior cusp of the aortic valve. The aneurysm measured 1.9 cm. in depth. Along the ventricular surface of the aneurysm there were cordlike structures which bore a resemblance to chordae tendineae. The tricuspid valve revealed a deformity (Fig. 1,*B*) that occurred at the junction of the septal and anterior leaflets. It was characterized principally by the unusual shortness of the leaflets. The septal leaflet of the tricuspid valve appeared to be continuous with the cordlike structures described earlier in this paragraph, being separated by the wall of the aneurysm.

In the lungs, there was necrosis and caseation of both upper lobes with multiple coalescing foci. In the gastrointestinal tract ulceration of the mucosa was present in the small intestine. Histologic examination of the lungs and intestinal tract revealed tubercles with epithelioid cells, Langhans' giant cells, and lymphocytes. Areas of caseation were present in the lungs and small intestine.

Case 2.—*Clinical Features.* The patient was a white man, age 60 years, at the time of first examination in March, 1941. At this time the main symptom was dyspnea due to acute pulmonary edema. The past medical history revealed that hypertension had been present for ten years. Since 1937 the patient had been conscious of tachycardia. Between 1937 and 1941 re-

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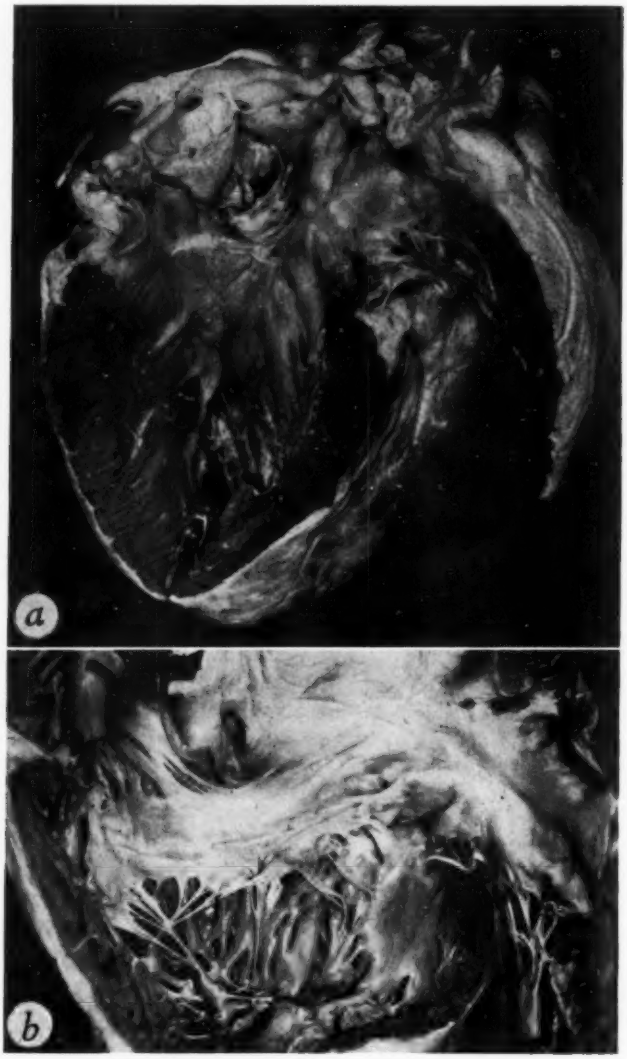
current episodes of paroxysmal auricular tachycardia, paroxysmal auricular fibrillation, and atrioventricular nodal rhythm had been recorded electrocardiographically elsewhere. No thoracic pain had been present, but a sense of substernal oppression associated with tachycardia had been observed by the patient. No preceding dyspnea had been observed. The family history revealed that the patient's father had died with diabetes; one brother had died with rheumatic heart disease, and one brother had suffered from heart disease of undetermined origin.

A.



B.

Fig. 1 (Case 1).—*A*. Aneurysm of membranous septum seen from left ventricle. *B*. Right ventricle. Shortness of leaflets of tricuspid valve at junction of septal and anterior leaflets.

The results of physical examination revealed an elderly white man, acutely ill. There was severe pulmonary edema. The pulse rate was 100 beats per minute. The blood pressure was 240 mm. Hg systolic and 110 diastolic. The examination of the thorax revealed moist râles bilaterally. The heart dullness extended to the midaxillary line. No murmurs were heard. The liver edge was palpable 2 fingerbreadths below the right costal margin. The extremities were normal.

The patient was immediately admitted to St. Anthony's Hospital, St. Petersburg, Fla. With oxygen therapy, ammonium chloride, digitalis, and restricted salt intake the patient responded favorably and was dismissed from the hospital in ten days.

The following laboratory work was done. Urinalysis revealed that the specific gravity of the urine was 1.015; the albumin determination was recorded as a faint trace; the sugar determination was negative; and on microscopic examination, a few hyaline and a few coarsely granular casts were observed. The complete blood count was within normal limits.

The electrocardiogram at this time showed the P-R interval to be 0.14 second and the QRS complex measured 0.08 second. The QRS complex was slurred in Lead II and it was notched in Lead III. The S-T segment was depressed in Leads I, II, and III. Diphasic T waves were present in Leads I, II, and III.

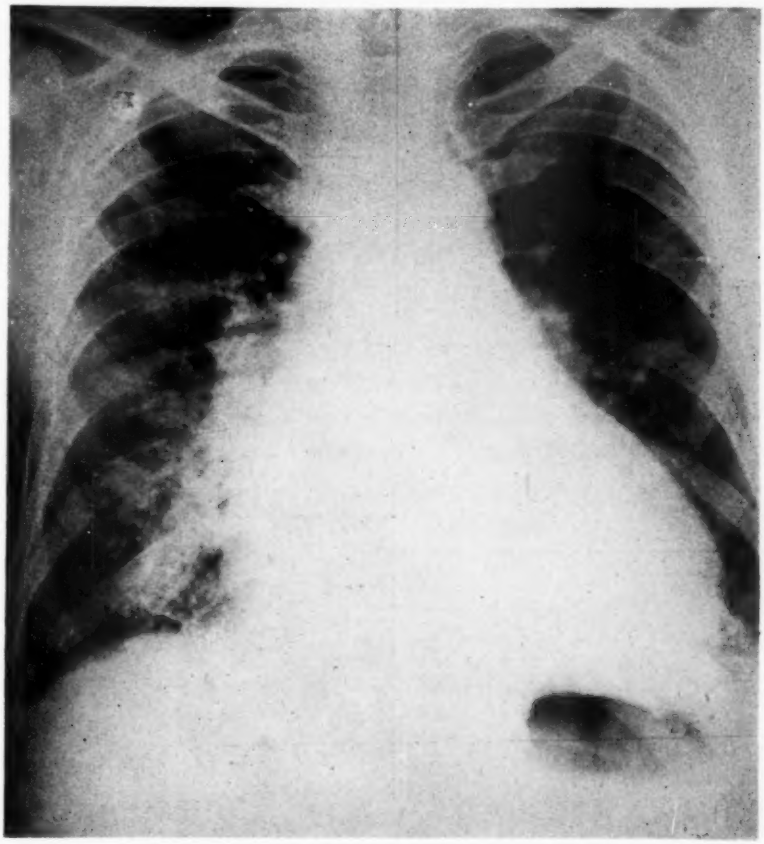
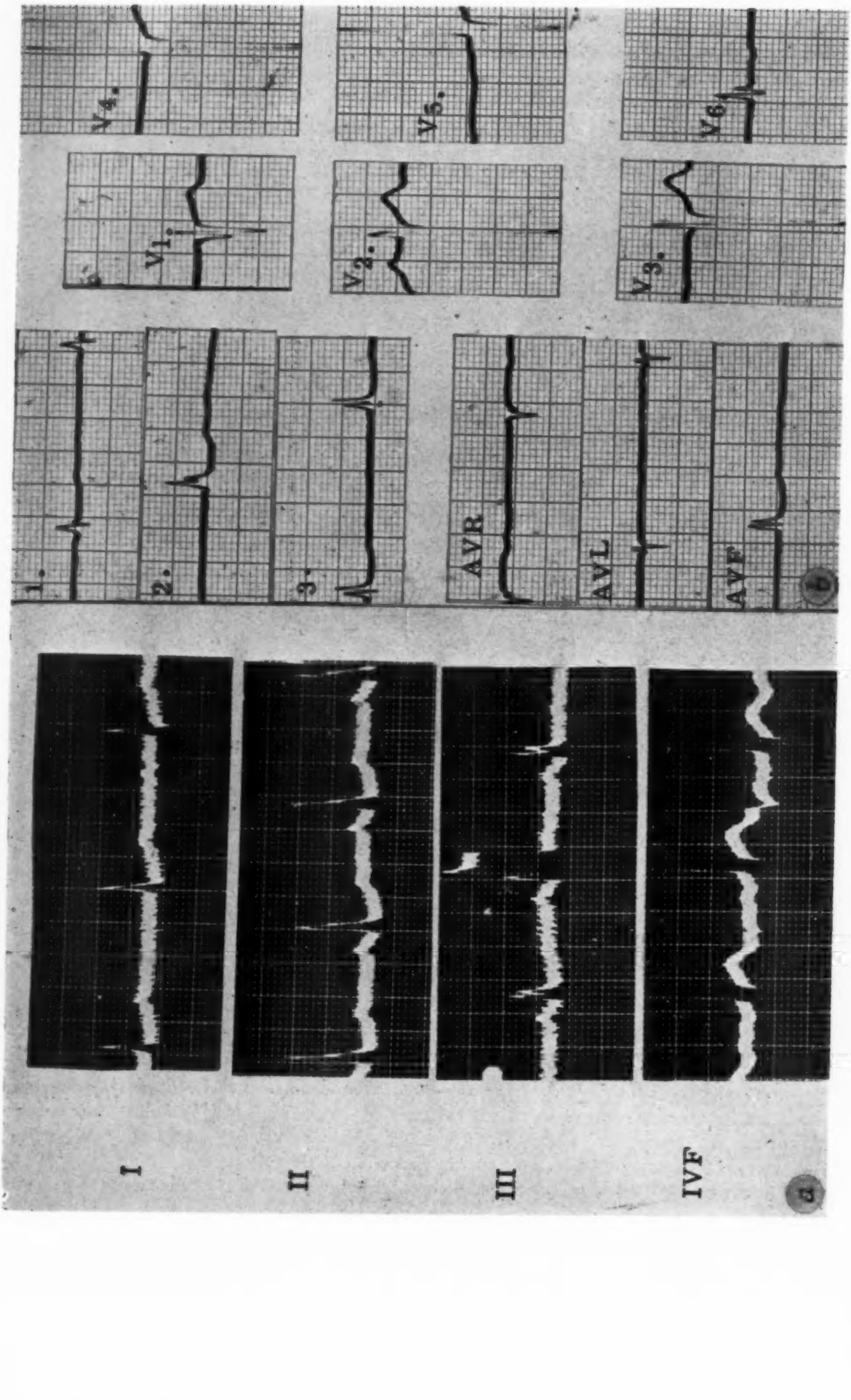


Fig. 2 (Case 2).—Roentgenogram of the thorax. Left ventricular enlargement.

During the next ten years the patient was examined at frequent intervals. He was very intelligent and cooperated fully with instructions concerning therapy. In October, 1943, he was hospitalized for ten days in view of increased evidence of congestive cardiac failure. His course was uneventful. In December, 1943, the electrocardiogram revealed a nodal rhythm with a short P-R interval measuring 0.08 second, but no alteration of the QRS complex. In May, 1944, paroxysmal auricular fibrillation was recorded electrocardiographically. At this time the patient was observed to have congestive cardiac failure, and mercurial diuretics were administered. Paroxysmal auricular tachycardia with an apex rate of 200 beats per minute was observed on several occasions in 1944. This was controlled with carotid pressure. In spite of the cardiac failure the patient was not an invalid. The summer of 1944 and each succeeding one were spent in Canada.



A. B.

Fig. 3 (Case 2).—Electrocardiograms. *A*, Sept. 17, 1946. Normal sinus mechanism. *B*, Nov. 9, 1905. Idioventricular rhythm.

In November, 1944, an idioventricular mechanism was observed with a rate of 40 beats per minute. The digitalis dosage was reduced slightly, and this was followed by an increase in pulse rate to 88 beats per minute. At this time the blood pressure was 230 mm. Hg systolic and 110 diastolic. In 1945 bronchopneumonia developed and the patient was rehospitalized. Roentgenographic examination (Fig. 2) of the thorax revealed marked enlargement of the heart. The transverse diameter of the thorax measured 31 cm., and the transverse diameter of the heart measured 18 cm. The cardiac-thoracic ratio was 59 per cent. An irregular density which was present in the mid-portion of the middle lobe of the right lung was interpreted as pneumonic consolidation. The patient responded well to therapy and continued in good health during the next year. An electrocardiogram in 1946 (Fig. 3,*A*) revealed normal sinus mechanism, with QRS changes similar to those described previously. Depression of the S-T segments in Leads I and II was present.

In February, 1947, the patient was seized with severe substernal pain, requiring atropine and morphine for relief. He was readmitted to St. Anthony's Hospital on Feb. 5, 1947, with a tentative diagnosis of acute myocardial infarction. At this time the pulse rate was 80 beats per minute and the blood pressure was 170 mm. Hg systolic and 110 diastolic. He was hospitalized for two weeks. Serial electrocardiograms revealed auricular fibrillation, but no changes consistent with acute myocardial infarction. There was depression of the S-T segment in Leads II and III consistent with digitalis effect. During the period of hospitalization, elevated temperature was not observed, but a leukocytosis of 13,350 per c. mm. of blood was present. The patient, after two weeks of rest in bed, was permitted to return by ambulance to his home, where two additional weeks of rest in bed were instituted. His course was uneventful. During the latter part of 1947 there were periodic episodes of sinus tachycardia. At this time administration of mercurial diuretics was required with increasing frequency to control evidence of pulmonary edema. The examination of the urine now revealed the specific gravity to be 1.018, with albuminuria, Grade I. The sugar determination was negative. The microscopic examination of the urine showed 6 to 8 coarsely granular casts per high-power field. The total serum protein was 6.7 Gm. per 100 c.c. of whole blood. A low sodium diet was again instituted. In the spring of 1947, phlebitis involving the left femoral and left popliteal veins had developed. This was treated with Dicumarol.

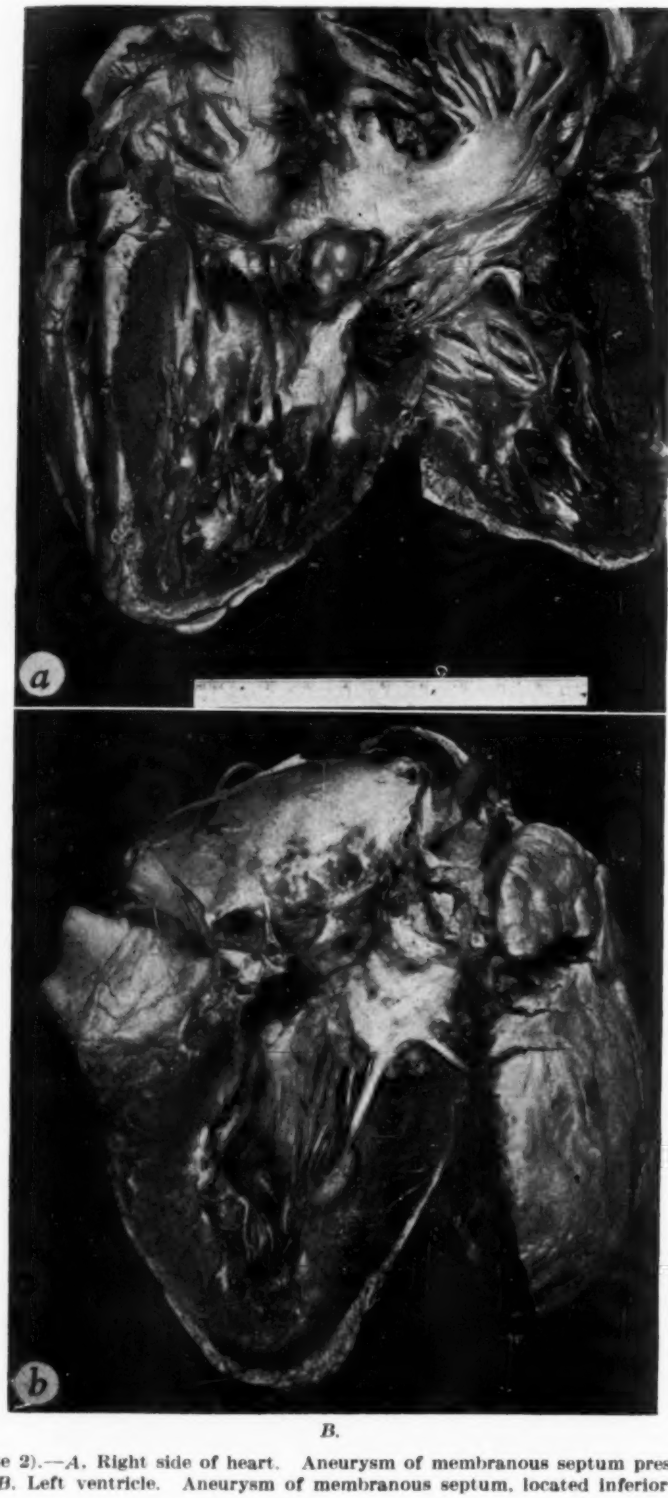
In November, 1948, the patient was readmitted to St. Anthony's Hospital with bronchopneumonia. Convalescence was uneventful. At this time albuminuria was Grade IV. Normal sinus mechanism was still present. Periodic episodes of congestive cardiac failure were observed. In 1949 administration of Mercaptomerin Sodium was instituted, which was continued at intervals of five to seven days until the time of the patient's death. In October, 1949, idioventricular rhythm developed and this rhythm persisted until the time of his death. During 1949 and 1950 the patient remained in good health, with evidence of cardiac decompensation well controlled with digitalis, ammonium chloride, and Mercaptomerin Sodium.

In November, 1950, there were no demonstrable changes in symptoms or in physical examination. The pulse rate was 76 beats per minute and the blood pressure was 180 mm. Hg systolic and 80 diastolic. No cardiac murmurs were observed. The electrocardiogram (Fig. 3,*B*) revealed an idioventricular rhythm. The T waves were of low amplitude or isoelectric in Leads I, II, III, aV_R, aV_L and aV_F. The T wave in Lead V_6 was inverted. The roentgenoscopic examination of the thorax revealed marked left ventricular enlargement but no fluid in the pleural cavities. The fundi revealed sclerosis Grade I plus. During the first three months of 1951 there appeared to be no appreciable change in the patient's general condition.

In April, 1951, dyspnea became increasingly severe; azotemia was evident at this time. The patient was readmitted to St. Anthony's Hospital on April 8, 1951. The physical examination at this time revealed a few râles at both bases. The pulse rate was 54 beats per minute and the blood pressure was 150 mm. Hg systolic and 100 diastolic. The liver was enlarged 2 to 3 fingerbreadths below the right costal margin.

The following laboratory work was done. The urine examination revealed the specific gravity to be 1.007. The albumin and sugar determinations were negative. The results of microscopic examination of the urine were normal. The erythrocyte determination was 4.7 million and the blood hemoglobin 14.5 Gm. per cent. The leukocytes numbered 10,200 per c. mm. The non-protein nitrogen determination was 133 mg. per cent. The creatinine determination was 5.1 mg. per cent. The blood chloride determination was 420 mg. per cent.

A.



B.

Fig. 4 (Case 2).—*A*. Right side of heart. Aneurysm of membranous septum presenting into the right atrium. *B*. Left ventricle. Aneurysm of membranous septum, located inferior to right aortic valve cusp.

In spite of therapy directed at azotemia, the patient did not respond and death occurred on April 11, 1951. His age at the time of death was 70 years.

Pathologic Features.—At necropsy the pertinent findings were confined to the heart, which was markedly enlarged, weighing 630 grams. There was an aneurysm of the membranous portion of the ventricular septum which presented itself into the right atrium (Fig. 4,*A*). The aneurysm on the right side of the heart appeared in the position of the anterior portion of the septal leaflet of the tricuspid valve (Fig. 5,*A*). Leaflet tissue as such at this location was not present. The edges of the aneurysm were continuous with tricuspid valvular tissue both anteriorly and posteriorly. The aneurysm was thin-walled, gray, and appeared to be composed of fibrous tissue. The right atrial portion of the aneurysm measured 2 cm. from before backward and 1.5 cm. in height.

On the left ventricular side (Fig. 4,*B*) the aneurysm appeared in the region of the membranous septum and its center lay inferior to the posterior portion of the right aortic cusp. A portion of the aneurysmal mouth was observed to lie inferior to the posterior aortic cusp (Fig. 5,*B*). The orifice of the aneurysm measured 1.8 cm. across and 1.5 cm. in height. The right aortic cusp appeared at its base to be continuous with the mouth of the aneurysm and the valve leaflet appeared contracted. The free edge of the posterior half of the right aortic cusp was thickened. There was no defect in the muscular portion of the ventricular septum.

A. *B.*

Fig. 5 (Case 2).—Aneurysm of membranous septum. *A*, Right atrium and right ventricle. Close-up view of Fig. 4,*A*. *B*, Close-up view of Fig. 4,*B*.

The right ventricular myocardium was hypertrophied and the wall measured 0.7 cm. in thickness. The left ventricular wall was also hypertrophied and measured 2.0 cm. in thickness. In the lower central portion of the ventricular septum there was thinning of the septum noticeable on the left side over an area of about 1.5 cm. The outward appearance of this lesion was consistent with an infarct. There was a severe degree of coronary arteriosclerosis involving the left anterior descending coronary artery. The right coronary artery was only mildly sclerotic. The interior of the right atrium was gray and the wall was thickened. The left atrium was normal. The foramen ovale was anatomically closed.

The surfaces of both kidneys revealed numerous superficial subcapsular cortical cysts. Diverticuli were present in the sigmoid colon. The aorta revealed widespread atheromatosis with ulceration.

Histologic examination of the heart revealed fibrosis of the ventricular septum in the sections through the lower middle portion, with smaller areas of fibrosis in the myocardium of the left ventricle. In sections of the lungs there was pneumonia. The sections of the liver revealed chronic

passive congestion. In sections of the kidneys there was thickening and hyalinization of some glomerular capsules. Some of the tubules were cystic and in others there was evidence of pyelonephritis. The renal vessels revealed arteriosclerosis involving the small and medium sized arteries.

The following anatomic diagnoses were made: bronchopneumonia (bilateral), pyelonephritis, congenital aneurysm of the membranous ventricular septum, chronic vascular nephritis, coronary arteriosclerosis (left anterior descending artery), and myocardial infarct (ancient).

COMMENT

Embryologically the membranous ventricular septum is derived in part from endocardial cushion tissue. Frazer[1] demonstrated that the pars membranacea was "made from the fused A-V cushions, the auriculo-vestibular part from the right end of the upper cushion, the interventricular part from the lower one, with some trabecular structure joining this from the proper interventricular septum." In a previous report by one of the present authors and Edwards,[2] closure of the atrioventricular canal was discussed. This closure is related to union of tissue from four sources: dorsal and ventral endocardial cushion tissue, primary interatrial septum and muscular interventricular septum.

Mall[3] concluded that aneurysms of the membranous ventricular septum are due not to endocarditis but to an anomalous position of the aorta which misplaces the membranous septum into a horizontal position. Lev and Saphir,[4,5] in their exhaustive study and review of the literature dealing with aneurysms of the membranous ventricular septum, concluded that in most cases the condition is congenital and that the most satisfactory embryologic hypothesis for this anomaly was that originally postulated by Mall. This included an abnormal direction of the ventricular and bulbar septa. These later authors amplified the hypothesis of Mall by considering the anomaly under discussion to be associated also with a mild form of transposition. These authors considered, as embryologic variants, (1) abnormal formation and fusion of the endocardial cushions, (2) abnormal formation and fusion of the bulbar cushions, and (3) abnormal position of the proximal bulbar septum in relation to the muscular ventricular septum.

An analysis of the data in the two cases of aneurysm of the membranous ventricular septum discussed in this report would cause us to be in accord with the hypothesis of the congenital origin of the condition upheld by Mall, Lev, and Saphir. It would appear that aneurysms of the membranous ventricular septum are the result of an abnormality in the atrioventricular endocardial cushion tissue. In this respect, congenital aneurysms of the membranous portion of the ventricular septum appear to be related, at least embryologically, to the defect classified as incomplete division of the atrioventricular canal with patent interatrial foramen primum (persistent common atrioventricular ostium). In the latter defect the apparent embryologic cause of the anomaly is failure of fusion of the atrioventricular endocardial cushions. Further similarity in embryologic development may exist between these two congenital cardiac anomalies: that is, incomplete division of the atrioventricular canal with patent interatrial foramen primum, and aneurysm of the membranous septum. In the case of aneurysm of the membranous septum recorded by Zadoc-Kahn and Cousin,[6] there was absence of interatrial septum. Likewise in the case of Reinhard[7] and the case of Tüngel,[8]

aneurysms of the membranous ventricular septum coexisted with developmental defects of the septum primum.

The cordlike structures observed on the left ventricular wall of the aneurysm in Case 1 bore a resemblance to chordae tendineae and thus they may presumably have been derived from the embryologic anlage of the tricuspid valve. This does not seem an unreasonable explanation of these cordlike structures. If so, their presence in the left ventricle could be correlated with an anomalous deviation to the right of the endocardial cushion tissue, which takes part in the closure of the ventricular septum. This eccentric fusion of the atrioventricular endocardial cushion tissue could account for a portion of valve tissue derived from embryologic anlage of the tricuspid valve being separated from the rest of the tricuspid valve by closure of the membranous septum and in turn sealed into the left ventricular wall of the aneurysm.

It is of interest that mongolism may be associated with different cardiac malformations caused by the alteration in one tissue of the embryo. In an analysis of data on fifty-five cases of incomplete division of the atrioventricular canal[2] with patent interatrial foramen primum, mongolism was recorded as having been present in seventeen cases and its absence was recorded or could be assumed in but eight cases. Mongolism is an associated occurrence in congenital aneurysms of the membranous ventricular septum. It was observed in the two cases of the anomaly that were recorded by Lev and Saphir and in Case 1 of this report. Aneurysms of the membranous ventricular septum are not common. Rae[9] observed this type of congenital aneurysm to be present four times in 3,000 necropsies. Lev and Saphir, in 1938,[5] reported two cases and in an exhaustive review of the world literature were able to find about seventy recorded cases. Leckert and Sternberg[10] in 1950 reported one additional example of this congenital cardiac anomaly. These authors were able to find only nine reported cases revealing this anomaly recorded in the English literature from 1900 to 1938. Vanecek[11] has also reported recently (1950) one additional case revealing this anomaly.

Congenital aneurysms of the membranous ventricular septum are for the most part of little importance to the clinician. However, certain pathologic features of these aneurysms, which should add to their importance, might be emphasized. These aneurysms may be the site of formation of thrombi (Guccione[12]). They may be the site of superimposed subacute bacterial endocarditis, or they may in rare instances perforate (Reinhard[7]). Aneurysms of the membranous ventricular septum may be a factor in the development of subaortic stenosis (Rae[9]). It has recently been observed by Leckert and Sternberg[10] that membranous ventricular septal aneurysms may be a structural factor in the production of aortic insufficiency. In the second case reported herein extreme cardiac irritability was observed. Auricular fibrillation, atrioventricular nodal rhythm, paroxysmal auricular tachycardia, sinus tachycardia, and idioventricular rhythm were observed and recorded electrocardiographically. The location of the congenital aneurysm, in the membranous portion of the ventricular septum, might presumably be a factor in the cardiac arrythmias that were observed. In 1947 this patient had clinical evidence of myocardial infarction. While this was not con-

firmed electrocardiographically during life, a small infarct of the ventricular septum was observed at necropsy. The arrythmias which were observed were more of a clinical problem prior to 1947, when the myocardial infarct was presumed to occur, than they were after this date.

Mongolism may give a clinical clue for the diagnosis of the anomaly under discussion. This finding was observed in Case 1, but in Case 2 the mental intelligence of the patient greatly exceeded normal.

SUMMARY

Two cases of aneurysm involving the membranous portion of the ventricular septum have been recorded. In Case 1 there were no associated clinical cardiac manifestations. In the second case there were many arrythmias which presumably were associated with the congenital aneurysm of the membranous portion of the ventricular septum. Mongolism was present in Case 1. The anomaly under discussion is probably congenital in origin. The possible relationship between two congenital cardiac anomalies—aneurysms of the membranous portion of the ventricular septum and incomplete division of the atrioventricular canal with patent interatrial foramen primum—is discussed.

REFERENCES

1. Frazer, J. E.: The Formation of the Pars Membranacea Septi, J. Anat. **51**:19, 1916.
2. Rogers, H. M., and Edwards, J. E.: Incomplete Division of the Atrioventricular Canal With Patent Interatrial Foramen Primum (Persistent Common Atrioventricular Ostium), Am. Heart J. **36**:28, 1948.
3. Mall, F. P.: On the Development of the Human Heart, Am. J. Anat. **13**:249, 1912.
4. Lev, Maurice, and Saphir, Otto: Congenital Aneurysm of the Interventricular Septum, J. Tech. Methods **16**:61, 1936.
5. Lev, Maurice, and Saphir, Otto: Congenital Aneurysm of the Membranous Septum, Arch. Path. **25**:819, 1938.
6. Zadoc-Kahn, L., and Cousin, M. J.: Sur un cas de malformation cardiaque congénitale. Absence de cloison interauriculaire. Diverticule borgne de la cloison interventriculaire, Bull. et mém. Soc. méd. d. hôp. de Paris **2**:1446, 1925.
7. Reinhard, Hans: Zur anatomischen und pathologischen Kenntniss der dünnen Stelle in der Herzscheidewand (Pars membranacae septi ventriculorum), Virchows Arch. f. path. Anat. **12**:129, 1857.
8. Tüngel, C.: Ein Fall von congenitaler zweifacher Perforation der Herzscheidewand; Tod durch Endocarditis un Embolie, Virchows Arch. f. path. Anat. **30**:267, 1864.
9. Rae, M. Viola: Congenital Aneurysm of Interventricular Septum Complicated by Subaortic Stenosis and Other Anomalies, J. Tech. Methods. **15**:136, 1936.
10. Leckert, J. T., and Sternberg, S. S.: Congenital Aneurysm of the Membranous Interventricular Septum With Unique Anomaly of the Pulmonary Vessels, Am. Heart J. **39**:768, 1950.
11. Vanecek, Emanuel: Aneurysma septi membranacei, Lék. listy **5**:597, 1950.
12. Guccione, F.: Quoted by Cannell, D. E.: Congenital Aneurysm of the Interventricular Septum, Report of Two Cases, Am. J. Path. **6**:477, 1930.

VENTRICULAR FIBRILLATION FOLLOWING EYEBALL PRESSURE IN A CASE OF PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

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PASSAIC, N. J.

THIS is the report of a case in which ventricular fibrillation followed the clinical application of eyeball pressure for paroxysmal supraventricular tachycardia. We believe it to be unique in the medical literature and feel that it is important to point out an unsuspected danger in an accepted and frequently utilized therapeutic procedure.

CASE REPORT

A 46-year-old, married, white housewife suffered the first attack of paroxysmal supraventricular tachycardia at the age of 18 years. The attacks were originally described as severe palpitation, usually occurring after bending down, disappearing spontaneously in a few minutes. These occurred at intervals of months to years. In 1933, an attack occurred lasting several hours. For the first time a physician was consulted who gave the patient an injection of morphine with complete relief in about one-half hour. This attack was accompanied by numbness in hands and feet. Following this, attacks occurred about twice a year. There was no longer any obvious precipitating factor. At least one attack began during sleep. Finally, in 1939, an attack was uncontrollable by morphine alone, and one of us (I.E.) was consulted. This attack was terminated by eyeball pressure. The patient was placed on quinidine sulfate 0.2 Gm. three times a day on which she has continued to the present. Several additional attacks occurred, all terminated by eyeball pressure except the last in which carotid sinus pressure was used successfully. The patient has been free from attacks in the past year. She underwent a hysterectomy in 1940 for fibroids and an appendectomy in 1936 for acute appendicitis, but has otherwise been singularly well throughout her life except for occasional gastrointestinal symptoms, thought to be on an emotional basis by her attending physician.

A number of laboratory examinations were done at various times. Numerous cardiograms in symptom-free intervals were always within normal limits (Fig. 1). Cardiac roentgenograms and fluoroscopy were always within normal limits. Several complete blood counts, urinalyses, and stool examinations were normal. Erythrocyte sedimentation rate, blood sugar, and basal metabolism rate revealed no abnormalities. A gall bladder and gastrointestinal series revealed no abnormality.

On Nov. 9, 1948, one of us (I.E.) was consulted by the patient for palpitation. She was found to have another attack of paroxysmal supraventricular tachycardia. Morphine sulfate 15 mg. was given subcutaneously, and, with a conventional photographic type of electrocardiographic apparatus attached to the patient, eyeball pressure was applied. The pertinent portion of the resulting tracing is shown in Fig. 2. Several runs of bizarre ventricular complexes, the longest of which included at least six, were interspersed with short periods of complete arrest, premature ventricular complexes, and normal sinus beats. The earlier part of the tracing reveals a typical supraventricular tachycardia at a ventricular rate of 210 per minute. The latter part of the tracing reveals a normal sinus rhythm with auricular and ventricular rates of 110 per minute and a P-R interval of 0.16 second.

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DISCUSSION

It is well known that vagal stimulation may cause slowing or even stopping of the normal or abnormal human heart. The heart reflex centers are in the medulla oblongata. In the dorsal nucleus of the vagus is found the cardio-inhibitory center, the neurone pool which gives origin to the efferent fibers of the vagus and also in which the afferent fibers of the vagus terminate.[1] Under ordinary circumstances, the activities of this cardio-inhibitory center and also of the cardio-accelerator center which result in the continuous discharge of impulses along the corresponding cardiac nerves are, in turn, dependent to a very large extent, if not entirely, upon the reception of impulses by afferent paths.

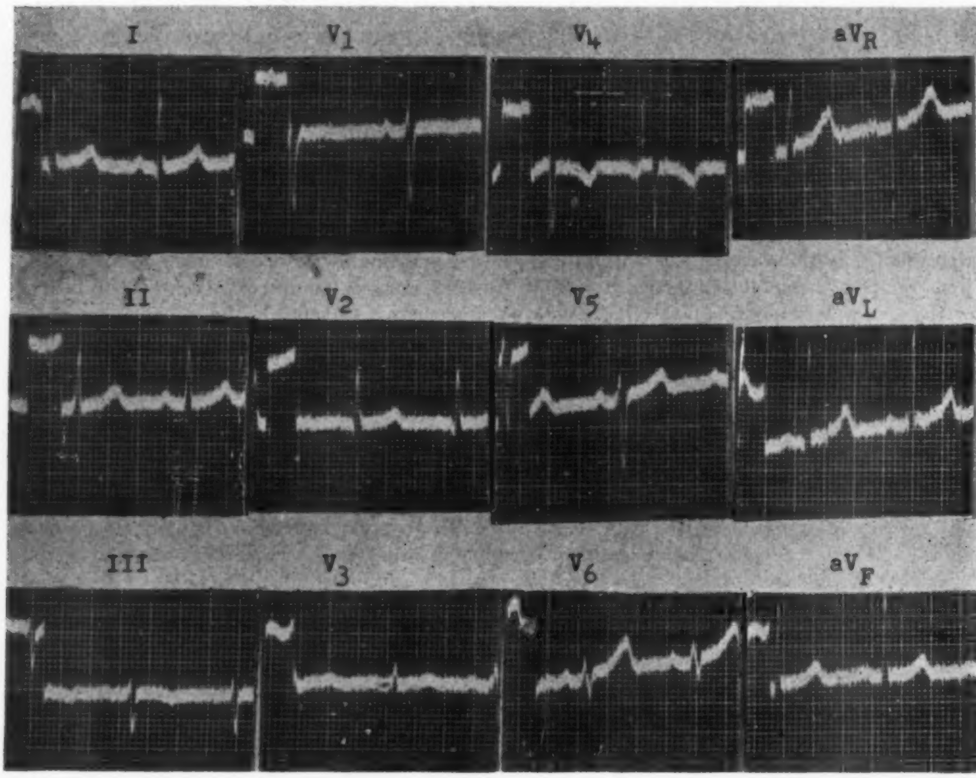

Fig. 1.—Electrocardiogram taken on May 11, 1950, revealing no abnormalities.

In other words, the maintenance of the tone of the centers which control the normal resting state of the heart and the alterations in rate which occur under various physiological conditions are in large measure either reflex in nature or due to impulses received from cerebral centers. The impulses which stream into the nervous centers arise in all parts of the body, the heart itself included. By these influences, the tone of either center may be exalted or depressed and corresponding changes produced in the cardiac rate.[2] Such a reflex arc is the oculo-cardiac reflex with its afferent arc in the ophthalmic fibers of the trigeminal nerve

and its efferent arc mediated through the vagus.[3] Another is the carotid sinus reflex with its afferent arc mediated through the ninth cranial nerve and its efferent arc through the vagus.

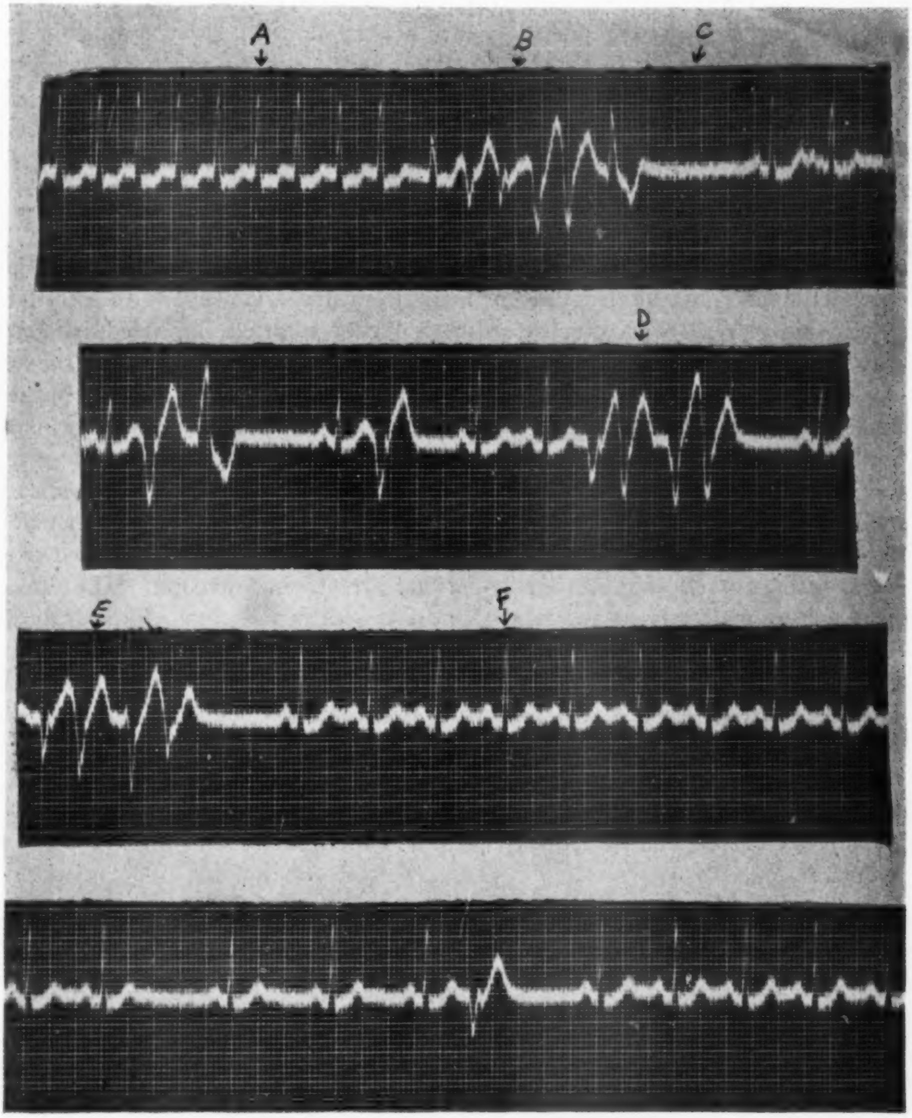

Fig. 2.—Electrocardiogram taken on Nov. 9, 1948. Consecutive tracing of Lead II. *A*, Eyeball pressure exerted during paroxysmal supraventricular tachycardia; *B*, *D*, and *E*, probable short runs of ventricular fibrillation; *C*, short period of complete arrest; *F*, return to normal sinus rhythm.

These facts have found clinical application to a considerable extent in the diagnosis and treatment of the tachycardias. Perhaps the single most important application has been found in the treatment of paroxysmal supraventricular tachycardia. The two methods commonly in use among clinicians for this

purpose are carotid sinus and eyeball pressure. They are described as being effective in an appreciable percentage of cases and as being quite safe if properly applied.[4-7]

There has been considerable interest in the carotid sinus reflex particularly in view of the numerous reports concerning the carotid sinus syndrome.[8-11] Three types of this syndrome have been described: a depressor type, a cerebral type, and a vagal type. The first two do not concern this communication. In the vagal type only have bradycardia or asystole with syncope been described. We know of no description of ventricular irritability (such as premature ventricular contractions or ventricular fibrillation) in this syndrome or for that matter in the therapeutic clinical application of carotid sinus pressure.

On the other hand, very little interest has been shown in the oculocardiac reflex, particularly in the English medical literature. However, an excellent study of this subject with electrocardiographic correlation appeared in *Folia Cardiologica* in 1941.[12] Sabena and Posteli in this study extensively investigated the oculocardiac reflex in normal and abnormal individuals. They found that the oculocardiac reflex causes, besides changes in heart rate, changes in myocardial irritability. The latter are manifested by extrasystoles or by suppression of the primary center of stimulus formation and activation of secondary centers, such as the node or the ventricle. Variations in the heart rate were easily demonstrable in 60 to 90 per cent of normal adults. The intensity of the slowing varied from slight to intense with culmination in cardiac arrest and syncope. The effects may appear immediately or be delayed. Of the variations in heart irritability the most characteristic are extrasystoles. Whereas experimental studies indicate that the vagus has the ability to reduce myocardial irritability, clinical observations reveal that instead of inhibiting extrasystoles, vagal stimulation will sometimes cause them to appear. In this study they were frequently found to appear after eyeball pressure. All types of extrasystoles including atrial, ventricular, and polymorphic were noted. The authors also noted conduction disturbances after eyeball pressure. These included partial to complete conduction block.[12]

In view of the bizarre and varied character of the individual complexes in the case presented here and the fact that one follows another without pause in the three runs marked *B*,*D*, and *E* on Fig. 2 (particularly *B*), it is the opinion of the authors that these runs represent true ventricular fibrillation rather than multifocal polymorphic ventricular premature contractions. In any case the differential does not alter the obvious inherent danger of sudden death in the situation. To the best of our knowledge no such case has been previously reported. The usual danger felt to be present in the use of vagal stimulation of the heart has been the possibility of complete cardiac arrest. To this must now be added the danger of myocardial irritability and ventricular fibrillation. Whether this represents a medical oddity or actually occurs more often than realized will be for further reports to decide. From the work of Sabena and Posteli[12] the possibility of producing myocardial irritability with fatal consequences by vagal stimulation does not appear too remote.

SUMMARY

A case is presented of a patient in whom eyeball pressure was applied to terminate an attack of paroxysmal supraventricular tachycardia with resulting short runs of ventricular fibrillation followed by return to normal sinus rhythm. The implication that myocardial irritability even to the point of ventricular fibrillation may be a hitherto unconsidered danger in the clinical use of vagal cardiac stimulation is offered.

The authors are indebted to Dr. Arthur C. DeGraff for his helpful suggestions.

REFERENCES

1. Evans, C. Lovatt: Principles of Human Physiology, Philadelphia, 1949, Lea & Febiger.
2. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, Philadelphia, 1949, Williams & Wilkins Company.
3. Friedberg, Charles K.: Diseases of the Heart, Philadelphia, 1949, W. B. Saunders Company.
4. White, Paul D.: Heart Disease, New York, 1944, The Macmillan Company, p. 873.
5. Lewis, Thomas: Diseases of the Heart, London, 1934, The Macmillan Company, p. 79.
6. Scherf, David, and Boyd, Linn J.: Cardiovascular Disease, St. Louis, 1941, The C. V. Mosby Company, pp. 313-314.
7. Levine, Samuel A.: Clinical Heart Disease, Philadelphia and London, 1945, W. B. Saunders Company, p. 193.
8. Smith, H. L.: Attacks of Unconsciousness Resulting From Hyperactive Carotid Sinus Reflex, AM. HEART J. **33**:711, 1947.
9. Crone, R. I., and Massey, F. C.: Carotid Sinus Syndrome, Northwest Med. **47**:585-587, 1948.
10. Wang, S. C., and Borison, H. L.: Analysis of Carotid Sinus Cardiovascular Reflex Mechanism, Am. J. Physiol. **150**:712-721, 1947.
11. Engel, G. L., Romano, J., and McLuis, T. L.: Vasopressor and Carotid Sinus Syncope; Clinical, Electroencephalographic and Electrocardiographic Observations, Arch. Int. Med. **74**:110-119, 1944.
12. Sabena, V. and Posteli, T.: Oculocardiac Reflex—Electrocardiographic Study, Folia cardiol. **2**:301-331, 1941.

HYPOPLASIA OF THE RIGHT AND THROMBOSIS OF THE LEFT CORONARY ARTERY WITH RUPTURE OF THE LEFT VENTRICLE: A CASE REPORT

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CHICAGO, ILL.

CARDIAC disease of adults associated with a developmental anomaly of the coronary arteries is rarely described. Only three reports have been found in which death was attributed to cardiac disease associated with hypoplasia of one coronary artery. The sudden development of extensive myocardial infarction with rupture of the left ventricle is uncommon in a healthy woman who has had no previous clinical evidence of cardiovascular disease. A case demonstrating all of these features is therefore of interest.

CASE REPORT

The patient was a 60-year-old white woman who was well until two hours before admission to the hospital. At this time she experienced severe nonradiating chest pain of sudden onset that was not relieved by two intramuscular injections of morphine sulfate, each $\frac{1}{4}$ grain. There was no history of diabetes or other chronic disease. Past history revealed that at the age of 49, the patient had acute cholecystitis for which the gall bladder was removed. At that time the blood pressure was 150/100 mm. Hg, the heart was of normal size to percussion, and there were no murmurs. X-ray picture of chest was normal and the electrocardiogram disclosed only a moderate left axis deviation.

Physical examination on admission revealed a temperature of 37.5° C., pulse 100, respirations 18, and blood pressure 160/100 mm. Hg. The patient appeared acutely ill. She complained of severe pain in the chest. The skin was moist, cool, and dusky and the nail beds were cyanotic. The chest was clear to auscultation and percussion. The respirations were shallow. Auscultation of the heart revealed sluggish sounds, a gallop rhythm, and no murmurs. The abdomen was soft and nontender and the liver was not palpated. The reflexes were hypoactive and equal.

The patient was placed in an oxygen tent but duskiness of the skin persisted. The blood pressure dropped to 120/80 mm. Hg, the pulse became weak, and nausea developed. The patient became deeply cyanotic and died sixteen hours after the onset of chest pain.

Autopsy.—The heart weighed 267 grams. The pericardial sac contained 275 c.c. of fluid and clotted blood. The epicardium was discolored dark red and the surface was roughened by fibrinous adhesions. The myocardium over the anterior apical surface of the left ventricle was soft and light brownish-red mottled with dark brown over an area measuring 2.5 cm. in diameter. In the center of this region there was a ragged vertical rent measuring 1 cm. in length through which a blunt probe passed into the cavity of the left ventricle (Fig. 1). Sections disclosed a pale brownish-red moderately firm myocardium throughout the right ventricle and remainder of the left ventricle. The endocardium was smooth, gray, and glistening except over the anterior apical surface of the left ventricle where there was a small ragged rent and a focus of subendocardial hemorrhage. There were no mural thrombi. The tricuspid, pulmonic, and aortic valves were thin, smooth, and translucent. The leaflets of the mitral valve were slightly thickened, gray, opaque, and disclosed minute vessels over the atrial surface.

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The left coronary artery arose from a large ostium in the left posterior aortic sinus and divided into a descending branch and a circumflex branch (Fig. 2). Cross sections disclosed pale yellow intimal plaques that moderately encroached on the lumens. The first portion of the descending branch of the left coronary artery revealed a pale gray mottled with dark red, firm adherent cut surface for a distance of 1.5 cm. through which a lumen was not identified. The large circumflex branch of the left coronary artery was patent throughout and extended around the atrioventricular sulcus to the posterior interventricular groove in which it descended to supply the posterior surfaces of the right and left ventricles (Fig. 1).

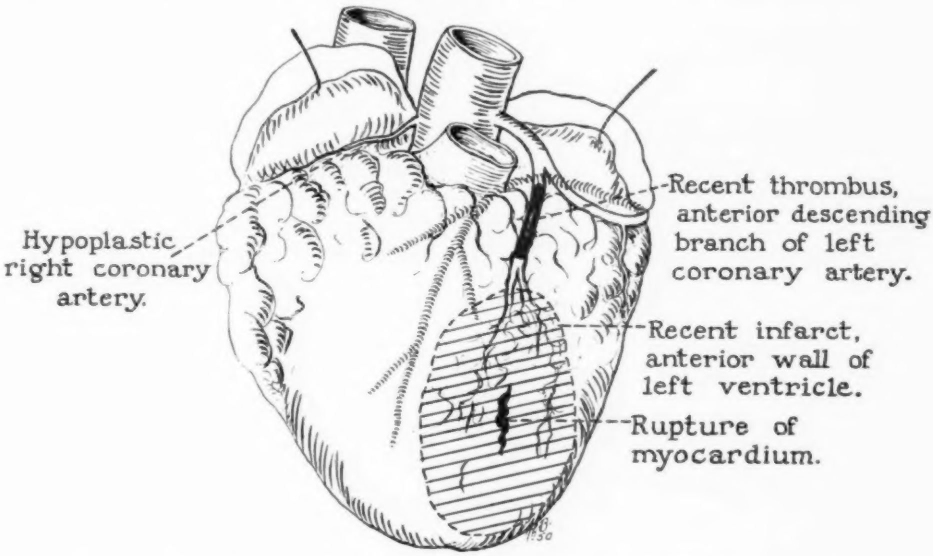

Fig. 1.—Diagram of heart showing hypoplasia of right coronary artery, thrombosis of anterior descending branch of left coronary artery, and recent infarct of myocardium with rupture.

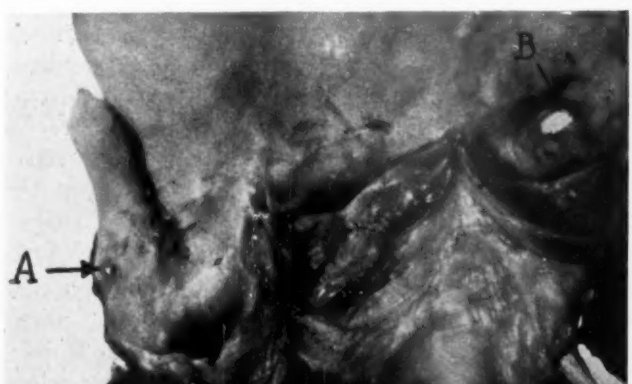

Fig. 2.—Aortic valve showing ostia of right (*A*) and left (*B*) coronary arteries.

The right coronary artery arose from a minute ostium measuring less than 0.1 cm. in diameter from the proximal aorta just above the anterior aortic sinus (Fig. 2). Cross sections disclosed

a minute vessel that could be followed for a distance of only 4 cm. The proximal portion would admit a fine probe for a distance of 1.5 cm. No other arteries were discernible over the anterolateral portion of the right ventricle.

Histologic examination of the right coronary artery revealed a small vessel from which minute patent branches arose. There was moderate concentric thickening of the intima by fibrous tissue. Sections of the descending branch of the left coronary artery disclosed marked encroachment on the lumen by a large arteriosclerotic plaque and a minute lumen nearly occluded by a recent thrombus that was adherent to the intima. Histologic examination of the myocardium revealed normal muscle except in the anterior left ventricle where there was necrosis, fragmentation of myofibrils, and extensive infiltration with polymorphonuclear leukocytes. The epicardium of this region was covered by fibrin.

The significant lesions were limited to the cardiovascular system. The final anatomic diagnoses included recent thrombus of the descending branch of the left coronary artery, hypoplasia of the right coronary artery, and recent infarction of the anterior left ventricle with rupture, hemopericardium, and cardiac tamponade. There was also arteriosclerosis of both coronary arteries with stenosis of the descending branch of the left. In addition, there were focal acute fibrinous epicarditis, healed nondeforming endocarditis of the mitral valve as well as moderate pulmonary edema, and slight focal arterial sclerosis of the right and left kidneys.

DISCUSSION

In 1945, Frachtman[1] stated that he had seen one case in which the right coronary artery was unusually small and poorly developed. The myocardium of the right ventricle was stated to be normal and death was due to thrombosis of the descending branch of the left coronary artery. An infarct of the left ventricle was not described and further details of the case were not reported. Whiting[2] described a 14-year-old white school girl who had rheumatic fever at the age of 6, developed angina pectoris at the age of 13, and died one year later in an episode of congestive heart failure. Autopsy examination revealed an enlarged heart weighing 425 grams, a large patent left coronary artery, and a rudimentary right coronary artery so small that the ostium would not admit a probe and the vessel could not be followed over the right ventricle. The posterior leaflet of the mitral valve was described as being "rudimentary." Histologic examination disclosed fibrosis and atrophy of the right ventricle and hypertrophy of the left ventricle. There was no infarct and rheumatic carditis was not seen. The third account of a case of coronary artery hypoplasia was reported by Wainwright.[3] He described a 14-year-old girl who died suddenly after an episode of extreme fright. Autopsy revealed a right coronary artery 1 cm. in length with an ostium that was "scarcely more than pinpoint in size." There was a small focus of fibrosis of the myocardium in the region normally supplied by the right coronary artery and the remainder of the myocardium was normal. This case was discussed by Dr. George McCallum[3] who stated that it was reasonable to assume that the focal myocardial fibrosis of the right ventricle was due to inadequate arterial blood supply. No other reports were found in which hypoplasia of a coronary artery was mentioned as a clinical or anatomic diagnosis.

Hypoplasia of the right coronary artery to the extent here described constitutes a heart that is functionally nourished by a single left coronary artery. The question arises as to whether the infarct of the myocardium would have been smaller and less serious if the right coronary artery had been normal. Dutra[4]

pointed out that there is no apparent functional or anatomic abnormality of the myocardium in cases of single coronary artery and he believed that this was due to the conversion of sinusoidal channels of the developing heart into coronary vessels. Also, in a recent review of forty-five cases of single coronary artery, it was stated by Smith[5] that signs and symptoms of decreased cardiac function were not described in any case in which autopsy examination revealed an otherwise normal cardiovascular system. He cited the autopsy examinations of twenty-seven adults with single coronary arteries and found only three in whom death was ascribed to coronary thrombosis and myocardial infarction. In one case the infarct involved both ventricles and in two cases the extent of the infarct was not described. Therefore, it cannot be said with certainty in the case here described that the state of hypoplasia of the right coronary artery contributed significantly to the large size of the infarct or to the ventricular rupture. However, since thrombosis of the anterior descending branch of the left coronary artery usually does not cause such an extensive myocardial lesion unless there is advanced arteriosclerosis of the other coronary vessels, it seems likely that the left ventricle would have been less affected if the right coronary artery had been normal.

SUMMARY

A case of an adult is described in which autopsy examination revealed hypoplasia of the right coronary artery, a recent thrombus of the anterior descending branch of the left coronary artery, and a large recent infarct of the myocardium with rupture, hemopericardium, and cardiac tamponade. It seems probable, although this statement cannot be made with certainty, that the state of hypoplasia of the right coronary artery contributed to the large size of the myocardial infarct with rupture of the left ventricle.

REFERENCES

1. Frachtman, H. J.: Congenital Anomalies of the Coronary Arteries, Hawaii M. J. **5**:72, 1945.
2. Whiting, W. B.: Angina Pectoris at the Age of Fourteen Associated With Congenital Rudimentary Right Coronary Artery and Rudimentary Posterior Cusp of Mitral Valve, AM. HEART J. **14**:104, 1937.
3. Wainwright, C. W.: Sudden Death Associated With Hypoplasia of Right Coronary Artery, Tr. Am. Clin. & Climatol. A. **56**:59, 1941.
4. Dutra, F. R.: Anomalies of Coronary Arteries. Report of Two Cases, With Comment on Dynamics of Development of the Coronary Circulation, Arch. Int. Med. **85**:955, 1950.
5. Smith, J. C.: Review of Single Coronary Artery With Report of Two Cases, Circulation **1**:1168, 1950.

Book Reviews

Kymographische Röntgendiagnostik. Zur Beurteilung Des Herzens in Beispielen. By Prof. Dr. Pleinkart Stumpf. Stuttgart, 1951, Georg Thieme, Verlag.

One-quarter of a century after his original paper dealing with roentgenkymography, Dr. Stumpf reviews his experience with this procedure in the clinical study of heart disease and presents it in the form of a monograph. In an interesting introduction he discusses the two main general causes of heart border motion, including (1) filling and emptying of the heart and (2) pendulum movement of the heart as a whole. After a short section dealing with the description of roentgenkymographs obtained from normal hearts, the majority of the volume deals with records obtained in various types of heart disease. There are sections dealing with valvular lesions, myocardial infarction, myocardial insufficiency, arrythmias (including extrasystolic beats and fibrillation), diseases of the aorta including aneurysm, as well as pericarditis. There is also a portion devoted to the diagnosis of chest tumors. The book is well illustrated and concisely written. It provides an excellent summary of the information to be obtained in diseased hearts by this method of examination.

H. H.

Electron Microscopic Histology of the Heart. By Bruno Kisch (in collaboration with Joan Bardet). New York, 1951, Brooklyn Medical Press, 106 pages.

This publication consists essentially of three previously published papers on the electron microscopy of cardiac tissues. Many of these electron microscopic observations of cardiac muscle correlate with those which have been observed with the aid of the light microscope. Apparently new details are given about the myofibrils, the sarcoplasm, and the vascular supply. The observations were made on fixed tissues; osmium tetroxide and potassium dichromate were used.

The myofibrils are classified into two types: Type A myofibrils are mainly unbranched cylinders that extend the length of the fibers and are composed of a succession of segments like a bamboo stick. In Type B, single myofibrils are observed for only a short distance because they anastomose with one another to form a relatively wide syncytial sheath. The details of the structure of the myofibrils and the changes occurring during their disintegration are described at length. Their relation to the sarcoplasm and the presence of formed elements (sarcosomes) in the latter are well illustrated. Of particular interest is the observation that small capillaries (blood?) penetrate the sarcolemma and are present between the myofibrils. This intrinsic blood supply of the cardiac muscle fibers was not observed in skeletal muscle similarly prepared. (If this observation is correct, it would go a long way toward accounting for the ability of the myocardium to extract a high percentage of the oxygen present in coronary arterial blood.)

The relation of the submicroscopic structure of the heart to cardiac physiology, particularly to the electrophysiology of the heart, is discussed at some length. However, this phase of the presentation is less objective than the purely descriptive histology. Possibly the author may be allowed some freedom in the play of his imagination on this "topic." The tendency toward the assertion of function from the description of submicroscopic details without direct verification of the inferences illustrates a frequently committed error in anatomical studies.

K. C. and A. B. H.

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